# The American Journal of DIGESTIVE DISEASES

An Independent Publication

### DEVOTED TO GASTRO-ENTEROLOGY AND NUTRITION

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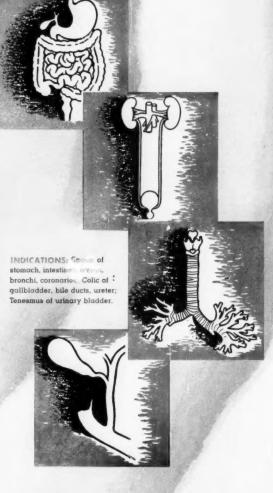
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# TREATMENT OF ULCERATIVE COLITIS WITH A FRACTIONAL COMPONENT OF HOG STOMACH EXTRACT

ROBERT EHRLICH, M.D.\*, Boston, Mass.

N a previous writing (1) a preliminary report was made of the treatment of idiopathic ulcerative colitis with a dessicated extract of hog stomach ("Ventriculin" Parke, Davis & Company), and it was stated that the postulate of an antiproteolytic substance present in the normal bowel precluded the development of ulcerative colitis, and that the deficiency of this substance rendered the patient susceptible to autolysis of the colonic nucosa by proteolytic enzymes. Therefore, the administration of a dessicated extract of hog stomach on the basis that it contained a protective or antiproteolytic substance seemed practical and was supported by the results of clinical improvement and recovery.

Stomach extract was used rather than intestinal extract since it was theorized that the stomach was more prone to autolysis than the small bowel and therefore normal stomach tissue should physiologically contain more anti-proteolytic substance. The potency of gastric enzymes over enteric enzymes has been substantiated by Driver (2) who stated that rennin and pepsin exceeded the ulcer producing effect of trypsin and erepsin on intestines of dogs.

This writing will, therefore, primarily concern itself with the clinical study of idiopathic ulcerative colitis as it relates to the treatment with a fraction of the dessicated hog stomach after a substantial part of the anti-anemic principle has been removed.\* Otherwise, it is physically similar to the whole dessicated stomach.

It seemed obvious that if the fraction of hog stomach containing the anti-proteolytic substance could be identified, it could be practically concentrated so that palatability and dosage of higher potency might render the method of treatment even more efficacious, especially in the fulminating type of case. Therefore, the fraction obtained from the hog stomach extract after the anti-anemic principle was substantially removed, was administered to a series of 24 cases of idiopathic ulcerative colitis to determine whether this fraction contained any of the anti-proteolytic substance, and if so, whether it was in greater or lesser concentration than the whole stomach extract.

Subsequent to the time of the last writing (1), it was decided to increase the dosage of the whole stomach extract to 100-120 Gm. daily. There were no untoward reactions, but rather, the period of recovery was short-

TABLE I Summary of Statistical Analysis of Cases Studied

Sex	50% Male		50% Female	
Age	30% 20-30 yrs.	45% 3040 yrs.	25% 40-50 yrs.	
Duration of Symptoms	30% 6 mo1 yr.	38% 1-3 yrs.	20% 3-5 yrs.	12% 5-15 yrs.
No. of stools Daily	33% 24	26% 4-8	29% 8-12	12% 12-20
Bleeding	17% none to variable	25% mild	41% moderate	17% marked
Degree of Ulceration	20% Stage I	29% Stage II	34% Stage III	17% Stage IV
Loss in weight	38% 1.5 lbs.	42% 5-10 lbs.	20% 10-20 lbs.	

\*Stage I - Diffuse hyperemia and friable mucosa on swabbing.

Stage II - Hyperemia, edema and miliary ulceration.

Stage III -- Mucopurulent sanguinous exudate, granular, and confluent ulcers,

Stage IV-Confluent ulceration, loss of haustral pattern. Poly, oid hyperplasia and structural deformity.

The author's concept of the pathogenesis was discussed in the previous report and, therefore, the rationale of the use of a hog stomach extract will not be referred to at this time, only to mention that continued clinical investigation and follow-up of the previously reported cases seems to further validate the anti-proteolytic concept and its application to therapy.

\*Assistant Surgeon, Rectal Clinic, Boston Dispensary.

ened and the incidence of relapse was nearly obviated. Therefore, this parallel study using a fraction of the stomach extract was carried out on this dosage schedule.

While this fraction was physically similar to the whole stomach extract, there was less complaint of

\* Material supplied by Parke, Davis & Company (Product Research Department).

unpalatability since the author found that it was preferable to place one heaping tablespoonful (10 Gm.) of the granules on the tongue and follow it by any desired liquid. In this way three tablespoonsful (30 Gm.) were consumed four times daily. Occasional complaints of gastric distress were eliminated by the simultaneous administration of dilute hydrochloric acid.

Here again, no comment was made to the patient regarding anticipated improvement, so as to in no way

influence his course by suggestion.

### PATIENTS STUDIED

A total of 24 cases were studied for a period of one year. The duration of the disease varied from six months to fifteen years, and the character of pathology from a diffuse inflammatory lesion to that of confluent ulceration and colonic deformity.

### CONTROL STUDY

The question arose as to whether the results obtained with the fraction of dessicated extract of hog stomach might be due to the high protein content, or whether resolution of the intestinal mucosa was the result of the anti-proteolytic substance. Therefore, an amount of protein hydrolysate, equivalent to the protein value of the extract of hog stomach, was administered to eight patients with idiopathic ulcerative colitis. The type of pathology was selected to parallel the group fed the fraction of stomach extract as closely as possible. The duration of administration varied from six weeks to three months, and averaged eight weeks.

The results were observed weekly by sigmoidoscopy and it was found that in all cases but one, bleeding, abdominal cramps and diarrhea persisted. However, in two cases, patients stated that they felt generally improved, but endoscopic observations revealed the ulcera-

tive process to be static.

This was further substantiated by Madden et al. (3) who stated that the administration of parenteral amino acids decreased the number of bowel movements, but when given orally bowel movements increased and at the end of the study, sigmoidoscopy still showed bleeding points and a reddened and edematous mucosa. Thus the results obtained with the fraction of dried stomach seems to be specifically dependent upon an anti-proteolytic substance.

It is wondered in the report of Machella and Miller (4) on "medical ileostomy" and the administration of amino acids whether the improvement of their patients was chiefly the result of the prevention of proteolytic enzymes or the substrate from contact with the mucosa of the large bowel, since blockage of the tube resulted in the presence of proteolytic enzymes and substrate in the colon with increase in the number of stools. By the same token their observation, and the above results of protein administration, would seem to further substantiate the fact that when proteolytic enzymes are not in contact with the ulcerated mucosa, resolution will result. The question then arises as to why those cases with surgical ileostomy do not always recover. In the light of two such cases which were treated with fraction of hog stomach, after not responding to surgical interruption of the bowel, and which then subsequently improved, it would seem that the antiproteolytic reserve had been exhausted and was inadequate to bring about resolution. In one case an ileitis complicated surgical recovery.

An additional control group of five cases which did not have ulcerative colitis but chronic diarrhea of indeterminate origin were administered the fraction of stomach to determine its effect on intestinal motility. This group did prove somewhat conclusively that some element of the material did depress motility to a normal state, and if the dosage were not minimized to 20-30 Gm. daily, constipation soon followed. Relapses of intestinal hypermotility were somewhat frequent, but were rather quickly controlled after a few days or a week of administration on therapeutic dosage. I would assume that the relapses were predicated upon the fact that the therapeutic period of administration was very short, and the very low maintenance dose was in-adequate. Whether the stomach extract contains any substance such as enterogastrone has not been determined by the author. In view of the above observation, it is not inferred that hog stomach extract should be indiscriminately used in cases of indeterminate diarrhea. One reason is that sensitivity to pork is moderately frequent in its occurrence, and in such case the diarrhea will be aggravated.

### RESULTS OF THERAPY

In this series antibiotic therapy was not resorted to as mentioned in the previous report in four cases, even though three fulminating cases were encountered. Likewise, of importance is the fact that no dietary restriction was placed on these patients. Their diets were neither low residue nor bland, and there was no vitamin supplementation or supportive therapy.

The results of therapy were evaluated primarily by proctosigmoidoscopic examination, and also by radiographic findings. It is interesting to note that only four cases required continuance of therapy after resolution had taken place. One case represented a history of 14 years of continuation before therapy; the second with a history of 10 years with a resultant deformity and stricture of the large bowel; and the third case, a markedly fulminating one, complicated by multiple fistulae. The fourth case, mild in character, of one year's duration, but because of low tolerance to the fraction (10-20 Gm. daily), required prolonged maintenance dosage. Two of these cases had some degree of relapse after therapy was discontinued for one to three weeks. The remaining two cases required readministration of the material when a mild relapse occurred about three months after cessation of original therapy. This is particularly interesting since I did not follow the pattern as in those cases in the preliminary report, in which a maintenance dose was used after resolution of the ulcerative process. The purpose being to procure an adequate reserve of anti-proteolytic substance. Thus the incidence of relapse (Table 2) is somewhat higher than might result when a routine maintenance dose is used. However, for contrast in the present series of twenty-four cases, medication was abruptly stopped when there was no further evidence of an ulcerating process. Apparently a physiological reserve is required in certain cases whereas in others it is not. In those cases having a relapse, it was promptly controlled within one to two weeks, and no further evidence of ulceration appeared. A point worthy of mention regarding the moot consideration of the relapsing-remission character of idiopathic ulcerative colitis is, that in the observation of the author, a remission not attended by therapy presented evidence on sigmoidoscopy of a degree of mucosal denudation, whereas those cases on therapy with hog stomach extract presented an intact, non-inflammatory mucosa. This important variation is significant since a symptomatic remission cannot be evaluated on a parallel with therapeutic "remission," where the latter is accompanied by a healed mucosa and the former was invariably not.

It was also noted that the more caudal the bowel involvement by ulcerating lesions, the higher and more prolonged was the dosage. This is consistent with the concept that the biologic endowment of antiproteolytic substance of the bowel decreases caudally, and therefore repletion of the substance and resultant healing predicates more intensive therapy.

tion has a more depressing effect on gastro-intestinal motility than did the whole stomach extract.

### Discussion

This study differs somewhat from that conducted with the whole hog stomach extract since in most cases only adequate material was administered to produce recovery and then medication was abruptly stopped in order to determine the ratio between dissipation of the anti-proteolytic reserve and the occurrence of a relapse. Likewise, the value of this study is emphasized by the fact that the patient's usual diet was not altered, and there was no supplementary or supportive therapy.

It was observed that relapses were more prone to occur in the cases of greater severity, indicating that the threshold of beginning depletion of anti-proteolytic reserve below physiological limits was more quickly attained than those cases of lesser severity. The conclusion is, therefore, obviously drawn that maintenance therapy beyond the point of recovery is an essential

TABLE II

Type of case	Stomach	of Dried Fraction ily)	% of Recovery in each group	Unimproved	Not Tolerated	% of Relapse in each group'
Mild (13%)	60-80	Gm,	100%		10% Urticaria Vomiting	20%
Moderate (33%)	100	Gm,	86%	14%‡		28%
Fulminating and Chronic continuous (54%)	120	Gm.	75%	25%	8% Diarrhea Aggravated	32%

<sup>\*</sup> Relapses were generally of short duration and aborted by re-administration of the dried stomach fraction,

Regarding those cases accompanied by severe gastrointestinal hypermotility with 15-20 stools daily, four cases were not favorably affected. It is rationalized that in such cases the rapid transit of the hog stomach fraction could not be adequately hydrolyzed and absorbed for maximum utilization. Perhaps when parenteral administration is posssible, this factor may be obviated.

Of three patients in the chronic and fulminating group that were unfavorably affected, was one fulminating case which did not tolerate the material and whose diarrhea became aggravated. A second patient was partially improved, but continued to lose weight, and since she was complicated by multiple fistulae and upper respiratory infections, ileostomy was resorted to. The third case did not follow through on treatment or re-examination and was classified as "unimproved." An additional case of ten years' duration did respond favorably, but due to multiple polyposis throughout the colon is now being considered for colectomy in view of the puestion of malignant degeneration.

The element of constipation was encountered in six cases shortly before administration was interrupted. This factor appears to be more predominant than in those cases treated with the whole hog stomach substance. It therefore appears that the hog stomach frac-

phase of treatment in order to effect and maintain colonic integrity.

Another interesting observation is that many of these patients were able to tolerate provoking emotional upsets and upper respiratory infections without relapse, which is so prevalent in the untreated patient. This was not always so remarkable in the originally fulminating case.

The incidence of constipation in several cases while on therapy, that did not previously experience constipation, is noteworthy, since it appears that some element in the fraction has a depressing effect on intestinal motility. Whether enterogastrone enters this equation has not been determined.

The incidence of gastro-intestinal allergy to pork with resultant aggravation of symptoms in three cases is a somewhat disconcerting factor, and of necessity eliminates such patients from this form of therapy. However, two of three cases were in the mild group (Table 2) and although one young male had a profound diffuse urticaria, he continued with the substance until resolution of the ulcerative colitis had taken place. The second patient experienced vomiting, gastric distress and distention, but also persisted until recovery. It is hoped that future study will circumvent this by eliminating allergenic properties. Likewise, large

<sup>#</sup> Patient still under treatment, but showing satisfactory progress.

dosage and some instances of unpalatability must be considered in dealing with the sensitive patient.

Finally, in the fulminating case, a more concentrated substance not necessitating such a degree of proteolytic cleavage may counter-balance the loss of hog substance in feces due to the extreme intestinal hypermotility.

From the foregoing study and analysis it seems evident to the writer that the fractional component of dessicated extract of hog stomach is generally better tolerated and its anti-proteolytic property is clinically more potent than the whole substance. However, there have been instances in which a patient was doing well on the "Ventriculin," and for comparative purposes, was placed on the fraction with resultant aggravation of symptoms and vice versa. Why this phenomenon exists, I cannot explain, but this variable selectivity does exist.

This study with a hog stomach fraction is perhaps but a phase in the transition of the progress in the development of an improved anti-proteolytic substance, but its present value in the treatment of ulcerative colitis is worthy of a definite place in the medical armamentarium. It further substantiates the concept of the proteolytic pathogenesis of ulcerative colitis, as reported by the author in a previous writing (1).

### SUMMARY

1. Treatment of twenty-four cases of idiopathic ulcerative colitis with a fractional component of descicated extract of hog stomach is herein reported. The type of cases encountered varied from mild to fulminating. There was no dietary restriction, and neither supplementary nor supportive therapy was used.

- It was determined by a control study that the increased protein intake in the extract did not apparently influence resolution of the ulcerative process.
- 3. Results of therapy were encouraging since 88% of the cases recovered. 25% of the cases in the fulminating or chronic continuous type were not improved, and 4% of the cases were aggravated due to the allergenic property of the extract.
- 4. The incidence of relapse was relatively greater than what actually may have existed, since maintenance dosage after resolution was not generally followed. Relapses, however, were usually controlled without difficulty on readministration for 1-2 weeks.
- It is felt that this substance is clinically more potent in its antiproteolytic substance than the whole hog stomach extract.
- This study further substantiates the proteolytic concept of the pathogenesis of ulcerative colitis.

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# ETIOLOGY AND PATHOGENESIS OF PROLAPSED GASTRIC MUCOSA INTO THE DUODENUM

ABRAHAM MELAMED, M.D., Milwaukee, Wisc.

THE condition of gastric mucosa slipping into the duodenum is rapidly gaining recognition as a frequent and significant cause of upper gastrointestinal discomfort. In our experience the incidence of prolapsing gastric mucosa is greater than benign gastric ulcer. Many theories are advanced to explain the development of mucosal prolapses of the stomach. It is not our intention to disprove any or all of these hypotheses; an attempt to apply and combine them in different instances is intended.

"Intussusception" of gastric mucosa represents an abnormal or pathologic state, either primary or secondary. That the stomach wall is subject to pathologic changes, often reversible, in systematic disorders is not ordinarily appreciated. Such an etiological background is responsible for some cases of slipping gastric mucosa.

Submitted March 26, 1949,

From Dept. of Radiology, Evangelical Deaconess Hospital, Milwaukee Wis.

Adapted from paper presented at Midwest Radiologic Conference, Milwaukee, Wis., February 6-7, 1948.

In any event, mucosal extrusions into the duodenum should not be treated lightly, witness such complications as hemorrhage and carcinomatous degeneration (1). In those patients with primary prolapses or those due to inflammatory states surgery has effected cures. Norgore and Schuler (2), Appleby (3), Scott (4), Manning and Highsmith (5) report complete relief of symptoms following subtotal gastric resection or extirpation of the hypermobile and redundant folds. Three of our patients were subjected to surgery and the results obtained in all were excellent.

This report consists of fifty consecutive cases of slipping gastric mucosa encountered in private practice and Evangelical Deaconess Hospital in a period of about three years. Of all organic disorders in the upper gastrointestinal tract duodenal ulcer is the only condition which we find to occur more frequently than slipping gastric mucosa. The incidence of extruding prepyloric mucosa in our practice is greater than the reports of Scott (4), Appleby (3), Manning and Highsmith (5). Our patients range in age from 17 to 69

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years, but most cases are found in the fifth decade (Table 1). Scott (4) reports seven of his fourteen cases in the fourth decade but his material is gathered from the military. The age distribution in the male and female groups is similar but the ratio is 4:1, respectively. All of our patients are white.

### TABLE I, AGE INCIDENCE

Age	Male	Female	Total
10-19		1	1
20-29	5		5
30.39	7	1	8
40-49	14	6	20
50-59	5	2	7
60-69	9		9
	10000	-	1000
	40	10	50 (White

Hypermobile and redundant prepyloric gastric mucosa may be classified according to the degree or extent of involvement (Table II). Those of long standing or large prolapses usually involve the entire circumference of the distal stomach.

### TABLE II. ANATOMICAL TYPES

- I. Prolapse involving portion of circumference of stomach. A. One prolapsing rugal fold.
  - B. Two or more prolapsing mucosal folds.
- 11. Prolapse involving entire circumference of stomach resulting in cuff-, mushroom-, cauliflower-, or "atomic-bomb"-like roentgen appearance.

Before alluding to the theories of pathogenesis and underlying etiological factors of slipping gastric mucosa it might be well to list the associated clinical or concomitant roentgen findings we encountered in a series of fifty cases. Some of these associated disorders or findings might have direct or indirect bearing on the development of slipping gastric mucosa (Table III).

### TABLE III. ASSOCIATED FINDINGS AND CONDITIONS IN FIFTY CONSECUTIVE CASES OF PROLAPSED GASTRIC MUCOSA

	No. of Patients
Generalized hypertrophy of mucosal patter Peptic ulcer	n of stomach 17
Duodenal bulb deformities	- +7
Duodenal ulcer crater	1
Gastric ulcer (benign)	1
Gall Bladder disease	5
Non- or poorly functioning	4
Cholelithiasis	1
Heart disease	3
Coronary heart disease without fa Congestive heart failure	ailure1 2
Nutritional disturbance pattern of small	intestine 2
Carcinoma of esophagus with blood protei	
Diverticulosis and/or itis of colon	3
Diaphragmatic hernia of stomach	9.
Gastrie diverticulum (pylorie)	1
Lymphatic leukemia (Marked enlargement	of spleen) 1
Trauma, occupation	3
Chronic alcoholism	9
Post-infectious hepatitis (?)	1

Prolapsing gastric mucosa represents an interesting if not fascinating, abnormal and/or pathological condition. Perusal of the literature reveals several theories concerning the etiology and pathogenesis of this condition. That the mucosa of the stomach is capable of active movement independent of contraction of the

muscularis is well established. Forsell (6) in 1923 is perhaps the first to describe such a phenomenon. More recently Brooks et al (7) find as a result of experimental studies in dogs that gastric mucosa is capable of movement due to contraction of the muscularis mucosa independent of the muscularis propria. Golden (8) believes that failure of the normal "stretching mechanism" of the mucous membrane during antral peristalsis is the cause of prolapse.

Eliason and Wright (9) claim that mild inflammatory states of the stomach lining can result in hypertrophy of the rugae. Subsequently these hypertrophied folds are forced into the duodenum by peristaltic waves. Many observers believe that hypertrophic rugae occur

only as the result of inflammatory states.,

Rees (10) suggests that prolapse of mucosa follows narrowing of the pyloric ring. Hyperperistalsis, loosening of the mucosa over the muscularis, and rugal hypertrophy supervene and result in extrusion of the mucosa through the pylorus into the duodenum. In our first case reported in 1943 (11) the pyloric ring admitted two fingers but the prolapse was immense. In our other two cases subjected to surgery the surgeon usually described the pylorus as "contracted." Most surgeons will confess, however, that a statement regarding the thickness or character of the pylorus at the operating table is hazardous indeed. A state of contraction or spasm during surgery might easily simulate hypertrophy or narrowing. Microscopic confirmation is wanting in such cases. Rees' conditions might obtain, at least, early in the disease, the pylorus eventually being "stretched" by the prolapsing membrane. Nevertheless, the thickened and/or contracting pylorus is capable of producing ischemia of the prolapsing portion of the gastric mucosa, eventually leading to ulceration and bleeding.

It is not difficult to comprehend the reasons for various opinions concerning the etiology and pathogenesis of slipping gastric mucosa into the duodenum. There are probably many etiological factors, one or more of which can be at play in the individual case. Notwith-standing meager knowledge and proof in some instances we shall attempt to segregate cases of extruding gastric mucosa on a pathologic basis (Table IV).

### TABLE IV. PATHOLOGIC CLASSIFICATION

### I. Primary

- A. Hypermobile rugae.
- B. Redundant, hypertropic rugae (?).

### II. Secondary

### A. Benign

- 1. Inflammatory,
  - a. Antral gastritis.

  - b. Hypertropic gastritis.
     c. Peptic ulcer (†).
- 2. Submucosal edema of stomach.
  - a. Congestive heart failure.
  - b. Hypoproteinemia; reversal of
  - albumin globulin ratio.
- 3. Idiopathic pyloric hypertrophy (Rees).
- 4. Miscellaneous.
  - a. Vitamin B. deficiency (†). b. Occupational; traumatic (!).

### B. Malignant

- 1. Carcinomatous degeneration (Rubin),
- 2. Lymphatic leukemia (?),

There is ample evidence on hand to believe that essential hypermobility of the prepyloric mucosa is the underlying cause of some cases of extrusion into the duodenum and that an inflammatory or spastic process in the antrum does not necessarily obtain. It is a rather common observation at the post-mortem table to be able to slide the mucosa over the muscularis of the stomach. The same conditions probably obtain in vivo. Mucosa is easily moved or stretched over muscularis during surgery of the stomach. Exaggeration of this "normal" phenomenon most likely represents conditions in the group designated as primary, hypermobile type. Roentgenologically there are no signs of inflammation and the rugae are not thickened. Roentgen studies in a typical case disclose a cuff- or mushroomlike prolapse of the gastric lining. In October 1945 we examined a 62 year old male who complained of anorexia and loss of 35 lbs. in one year. One year previously gastrointestinal roentgen studies elsewhere were reported as essentially negative. Our roentgen studies disclose a "sun-burst" or cuff-like prolapse of the prepyloric mucosa into the base of the duodenal bulb (Fig. 1). No evidence of rugal hypertrophy, spasm or ulceration is seen. Gastric motility was not delayed.

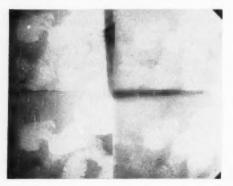


Figure I.—Mr. L. L., age 62. Serial x-ray views of the distal stomach and duodenum disclose umbrellalike deformity in the base of the duodenal bulb. Ragal markings are seen extending from the stomach into the duodenum. Primary hypermobility of the prepylorie nucess is probable underlying cause.

No one can deny that there is great variation in size of gastric rugae. Only gross deviations from the "normal" can be appreciated by examining fixed specimens. Although hypertrophy of gastric rugae is usually the result of inflammation there are instances where abnormally large gastric folds are due to congenital or developmental anomalies. In this respect the case report of Moersch and Weir (12) is interesting. Two large redundant folds of gastric mucosa exhibiting microscopic changes of chronic gastritis were found in the middle 1/3 of the stomach near the greater curvature and on the posterior wall, simulating neoplasm. Broders (12) believes these extremely large folds represent a developmental anomaly. The remainder of the stomach exhibited evidence of atrophic gastritis. Such rugae, if situated near the

pylorus, can easily be carried along or extruded into the duodenum.

In our present state of knowledge regarding prolapsing gastric mucosa one is unable to formulate infallible criteria to differentiate between primary and secondary types of prolapses. It is important, however, to recognize that systematic disorders such as hypoproteinemia, congestive heart failure, etc., are capable of creating pathologic changes permitting the development of slipping prepyloric nucosa. Such changes are reversible but where prolapses are primary or due to inflammation surgical measures are available which in all reported cases have provided cures.

Antral gastritis is perhaps the most important inflammatory state associated with and/or responsible for slipping gastric nucosa. The x-ray illustrations contained in the papers of Vaughan (13) Arendt (14), Pollard and Cooper (15) depict "intussusception" of the inflamed and redundant gastric nucosa.

Scott (4) alludes to the coexistence of peptic ulcer and herniating gastric mucosa. He regards prolapses incidental to peptic ulcers and observes that discomfort is present even after "healing" of the ulcers. We believe there might be common denominators in the etiology and pathogenesis of "herniating" gastric mucosa and peptic ulcer; the rate of coexistence of these lesions is greater than can reasonably be expected on a coincidental basis. 9 of 50 patients in this report exhibit evidence of peptic ulceration, acute and chronic-almost 10%. The youngest patient in our series, age 17 years, showed evidence of a chronic duodenal ulcer. She entered the hospital complaining of vomiting one half hour after meals for a period of one month. Nausea did not precede the vomiting and the vomitus often contained undigested food. In this patient no ulcer crater is visible but a marked duodenal deformity and slight prolapse of gastric mucosa into the duodenum are observed (Fig. 2, a and b).

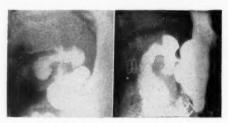


Figure 2, a and b—Miss D. G. age 17. a. Spot film discloses an atomic bomb-like defect in the base of the duodenal bulb, characteristic of prolapsing gastric nucosa. b. More complete filling of the duodenal bulb shows marked deformity due to chronic duodenal ulcer. No cratter is seen.

Benign gastric ulceration was found in another patient, a 45 year old male, who complained of vomiting for 1½ weeks, but experienced a similar episode 8 months previously. Roentgen studies disclose an ulcer, most probably benign, along the lesser curvature near the incisura angularis, marked hypertrophy of the gastric rugae and prolapse (Fig. 3, a and b). Is hypertrophic gastritis the underlying cause of ulceration and slipping mucosa in this patient?

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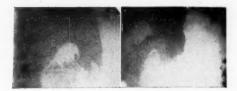


Figure 3, a and b—Mr. R. C., age 45. a. and b. Roentgenograms dated October 23, 1946 disclose marked thickening of the gastric rugae, gastric ulceration along the lesser curvature slightly above the level of the incisura angularis, and slipping of the redundant nuceosa into the duodenal bulb.

Submucosal and mucosal edema of the stomach secondary to congestive heart failure can give rise to slipping of the gastric mucosa into the duodenum (16). Reversibility of this condition is implied, depending on the state of circulation. We have encountered four such cases (Melamed and Melamed (16)); two are included in the present series. One patient in this group is extremely interesting. This 64 year old male luetic with congestive heart disease complained of indefinite gastrointestinal symptoms for about four months. Roentgen studies disclosed gastric mucosa slipping into the duodenum. Increased density in the left lower lung was seen during fluoroscopy. Further investigation was recommended, but the referring physician attributed the fluoroscopic findings to heart disease and fluid in the chest. Reexamination of the upper gastrointestinal tract 4 months later, after two severe bouts of decompensation and fibrillation and finally compensation, showed no signs of the previously demonstrated prolapse. A few months later this patient succumbed to pneumonia and primary tumors of the pancreas and lung (left lower lobe). Post-morten examination showed no evidence of prolapsed or redundant mucosa of stomach. No microscopic sections of the stomach wall were obtained at another hospital where the patient expired. Such a case provides adequate explanation-prolapse of edematous, pendulous and hemorrhagic stomach rugae—for at least some of the "gastrointestinal" complaints in congestive heart disease (16),

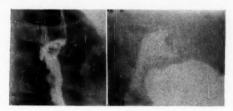


Figure 4, a and b—Mr. E. B., age 45. a. Esophagram discloses stenotic lesion in middle third of the esophagus due to squamous cell carcinoma. b. Prolapse of gastric mucosa into the base of the duedenal bulb. Prolapse believed to be due to starvation hyporoteinemia.

It is well established that changes in the blood proteins are often reflected in the wall of the gastrointestinal tract. Whether it be hypoproteinemia or re-

versal of the albumin-globulin ratio the effect, at least physiologically speaking, is similar to congestive heart failure. Although the mechanism differs from congestive heart disease blood protein changes give rise to the formation of edematous and pendulous gastric folds. A male patient, aged 45 years, had difficulty in swallowing for 6-8 months before seeking medical advice in January, 1947. This patient lost at least 45 lbs. A stenotic lesion of the esophagus due to squamous cell carcinoma was discovered by esophagram (Fig. 4, a) and esophagoscopy. A sufficient quantity of opaque media entered the stomach to permit disclosure of a large prolapse of the gastric mucosa into the duodenum (Fig. 4, b). All of the gastric rugae were thickened. Although no blood chemistry studies are available in this case there is every reason to believe that the underlying cause of the edema and prolapse of the gastric rugae is a state of starvation hypoproteinemia. Recent blood protein studies in a few patients with carcinoma of the esophagus showed reversal of the albumin-globulin ratio.

Scott (4) stresses the strong neurogenic factor in gastrointestinal disturbances including slipping of the gastric mucosa. The evidence in our patients is equally as convincing. Several of our patients report that emotional disturbances, lack of sleep, periods of stress and strain result in exacerbations. Pylorospasm and/or hypertrophy of the pylorus eventuate in exaggerated peristaltic waves and slipping of redundant folds or hypermobile folds into the duodenum (Rees (10)). We have followed the case of a middle-aged female physician since 1944. The condition of slipping gastric mucosa has been present for a period of at least 10-15 years. She states unequivocally that emotional unrest and the like terminate quite promptly in a feeling of fulness or "knotting" in the epigastrium, radiating to the back. Antispasmodics and sedation afford relief. Roentgen studies at various intervals always disclose prolapse of the mucosa but varying in degree. During exacerbations the mucosal pattern of the prepyloric mucosa is markedly edematous (Fig. 5, a) while in a relatively quiescent stage the mucosal folds are of



Figure 5, a and b—a. Compression studies of the antral portion of the stomach on January 7, 1944, during exacerbation, show marked edema or swelling of the rugae. b. Comparable studies on April 26, 1947 during quiescent stage, show relatively normal mucosal rattern.

normal thickness (Fig. 5, b). Perhaps this case is rightfully classified as antral gastritis.

There is no evidence to substantiate the compensatory aspects of trauma in the causation of slipping gastric mucosa. Two patients claimed trauma was the causative factor. In one the trauma was a sudden and direct blow to the abdomen while the other patient is engaged in work requiring frequent bending. The only possible association that might be drawn is that pylorospasm, initiated reflexly by trauma, in the presence of hypermobile gastric rugae, will eventually result in slipping of the mucosa into the duodenum.

In two other patients abnormal small bowel patterns were discovered. Clinically there were no signs of non-tropical sprue, tuberculosis, non-specific enteritis, etc. Further information could not be obtained but there is a slim possibility vitamin B deficiency was present.

Rubin (1) reports carcinomatous degeneration in a prolapse of gastric mucosa. While we have no proof at this time, it would not surprise us to discover subsequently that patients with untreated primary or inflammatory type of prolapses are more prone to such development than a control group. The period of observation of these patients is as yet most inadequate but this aspect is worthy of further study. One cannot entirely disregard the factor of chronic irritation which over a period of years might initiate cellular changes of neoplastic nature.

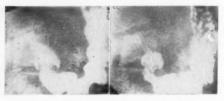


Figure 6, a and b—Mr. R. L., age 65. a. Patient with chronic lymphatic leukemia shows prolapse of gastric mucosa into base of duodenal buib. The gastric rugae are thickened (March 19, 1947). b. Similar findings are present in the stomach and base of the duodenal bulb five months later (August 2, 1947). Deep x-ray therapy to spleen brought white blood cell count to normal without any appreciable effect on roentgen appearance of stomach.

Mucosal prolapse was observed in a patient afflicted with chronic lymphatic leukemia. This male patient, aged 65 years, exhibited splenic enlargement during the course of an annual employment examination. Questioning of the patient disclosed indefinite upper gastrointestinal complaints ordinarily encountered in leukemia patients and attributed to splenic enlargement, liver involvement, etc. Roentgen studies of the abdomen and gastrointestinal tract were requested, however, with interesting results. The stomach was displaced to the right by the enlarged spleen. The rugae of the stomach show marked thickening and the prepyloric folds slip through the pylorus into the duodenum (Fig. The blood findings on March 19, 1947, were as follows: 16.5 Gms. hemoglobin (107%): 5,300,000 erythrocytes per c.mm.; 52,400 leucocytes per c.mm.; neutrophiles 20%, lymphocytes 80%, many basket cells. Deep x-ray therapy to the spleen of this patient was followed by considerable regression of the spleen and improved "general" condition but the patient still complained of occasional bouts of upper gastrointestinal discomfort. X-ray studies five months later show no appreciable change in the roentgen appearance of the stomach or duodenum (Fig. 6, b). The blood picture was markedly improved: 15.5 Gms. hemoglobin; 4,650,000 erythrocytes per c.mm.; 9,300 leucocytes per c.mm. with 52% lymphocytes. The coexistence of prolapsed gastric mucosa and chronic leukemia seems coincidental but one cannot entirely exclude leukemic involvement of the stomach, mucosal and/or submucosal.

Scott (4) discounts microscopic findings of cellular infiltrates as being of no etiological significance in prolapsing gastric mucosa. He does not believe inflammation is a causative agent. Although signs of inflammation might represent the result rather than cause of prolapse, some inflammatory states such as antral gastritis, hypertrophic gastritis and the like give rise to or are associated with prolapsing gastric mucosa. In at least 1/3 of our 50 patients the radiographic pattern of the gastric mucosa was such to indicate generalized hypertrophy of the rugae. There seems little reason to doubt that hypertrophic gastritis was present in many patients.

Three patients in this series of 50 were subjected to surgery. In two patients the microscopic changes were consistent with a diagnosis of chronic granular gastritis. A male World War II veteran, aged 35, complained of epigastric pain, "gas," vomiting and back stools on occasions. Gastroscopic examination at the Veterans Administration disclosed "hypertrophic gastritis." Roentgen studies show marked hypertrophy of the gastric rugae and a large prolapse Fig. 7, a). The symptoms eventually became so severe that the patient lost weight and could not work. The only recourse was surgery, following which the patient was cured. Surgery consisted of resection of the redundant and inflamed mucosa. The surface of the resected mucosa is intact but there are increased cells between the glands. In the muscularis mucosa there are scatterings of inflammatory cells-lymphocytes, eosinophiles and neutrophiles (Fig. 7, b).



Figure 7, a and b—Mr. H. B., age 35. a. Roentgen examination in March, 1947 discloses large prolapse of the gastric mucosa into the duodenum. Gastroscopic findings consistent with diagnosis of hypertrophic gastritis. b. Microscopic sections of resected redundant mucosa show chronic granular gastritis.

Another case subjected to surgery was that of a 54 year old female, first examined by roentgen means in 1944. At that time her complaints consisted of epigastric fulness or "gas" and 15 lb weight loss. Serial studies disclose slipping of the prepyloric mucosa into the duodenum (Fig. 8, a). Antispasmodics and modified diet afforded some relief but symptoms recurred in December 1946. A few months later recourse to

surgery was required. Here, too, simple resection of the redundant gastric lining was performed and the end result is depicted in roentgenograms taken in October 1947 (Fig. 8, b). There is no visible evidence of mucosal extrusion and no symptoms are present. The microscopic appearance is similar to the case described above, i. e., chronic granular gastritis (Fig. 8, c).

fibrosis. The bases of the ulcers show highly cellular granulation tissue and are covered by necrotic debris.

### SUMMARY AND CONCLUSIONS

The etiological factors of 50 conservative cases of prolapsing gastric mucosa into the duodenum are considered. On the basis of a review of the literature and



Figure 8, a, b and c—Mrs. B. W., age 54 a. Barium meal studies in March 1944 show slight to moderate protapse of gastric mucosa into duodenum. No peptic ulceration is present. b. Reexamination in March 1947, following surgical extinuation of the redundant mucosa, shows no evidence of slipping of the mucosa into the base of the duodenal bulb, c. Microscopic sections of the surgical specimen show chronic granular

The largest prolapse encountered in our series was reported in 1943 (11). The patient, 39 years of age, called the physician for treatment of bruises sustained after fainting. Later she admitted having passed black stools for three months. The blood hemoglobin was 3 grams. After administration of blood transfusions and detection of a prolapsing lesion in the stomach by roentgen means, surgery was performed. The surgical specimen, consisting of prolapsing polypoid mucosa, measured 6x9 cms. and showed two large ulcer craters. The sites of the ulcers correspond to the points at which the pyloric ring contracted down around the immense prolapsing mass. Ischemic necrosis resulted in almost fatal bleeding from these two ulcers.

Figure 9-Mrs. P. S., age 39. Microscopic section through portion of prolapse bearing larger ulcer crater shows edema and cellular infiltration of the mucosa, submucosa and muscularis mucosa. A background of early fibrosis present. Necrotic debris covers base of ulcer.

Microscopic section (Fig. 9) shows edema and cellular infiltration in the submucosa, muscularis mucosa and mucosa. In some places a few muscle bundles are separated by this tissue with a background of early

personal observations classification of such mucosal prolapses is attempted and proposed. Primary and secondary types of mucosal slipping are described.

Extrusion of prepyloric mucosa into the duodenum is capable of producing considerable discomfort, not infrequently necessitating surgical intervention. Surgical extirpation of the redundant mucosa was neces-sary in three cases. The microscopic findings are presented.

There are many causes of gastric mucosa slipping mo the duodenum. Attention is directed to those cases in which slipping mucosa represents one of the manifestations of systemic disease, in which instances the changes are reversible.

In our experience the incidence of prolapsing gastric mucosa is second only to duo lenal ulcer. The frequency of coexistence of peptic ulcer and prolapsing gastric mucosa in our group of 50 cases is almost 10%, suggesting some common etiological factors. Patients with slipping gastric mucosa warrant close observation. The possible relationship of this condition to carcinoma of the stomach is mentioned.

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### PHYSICS IN INTESTINAL INTUBATION

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THE ability of a surgeon to pass an intestinal decompression tube of radio-opaque rubber far down the gastro-intestinal tract of patients with bowel obstruction or paralysis of the bowel has been responsible for a vast number of lives being saved. A tremendous amount of effort went into the development of such tubes and into the methods by which they are successfully passed. It was only inevitable that different workers had different concepts of how such tubes moved down the gastro-intestinal tract, and naturally they patterned their tubes upon their own concept of its downward progression. In general, there are only three main types of intestinal tubes in use today.

The first of these tubes is the air-propelled decompression tube (1). This tube is based upon the concept that if the bowel in front of a balloon is decompressed and then if the balloon is inflated with air, that the stretching of the wall of the bowel by the inflated balloon would cause peristaltic movements to be initiated that carried this type of tube down into the gastro-intestinal tract. These workers designed a double-lumen tube to conform to their concept of its downward progression. This double-lumen tube had a fenestrated metal tip whose function it is to suction out the bowel in front of a rubber balloon of latex rubber which is fastened along and around the shaft of the tube behind the metal tip. One channel of the doublelumen tube communicates with the balloon so that it may be inflated or deflated and the other channel communicates with the fenestrated metal tip which is used to suction out the bowel. In addition to the fenestrated tip there are two small holes behind the balloon. These are also used to suction out the bowel. These workers are of the opinion that only two holes are sufficient behind the balloon because more holes would impair the decompressing effect of the tube.

The second type of tube is based upon using a weighted substance as lead or mercury (2) which is placed into the balloon of the tube. To use mercury as weight, this type of tube has the balloon fastened along the shaft of the tube just as in the air-propelled type of tube. The shaft through the middle of the balloon so restricts the free-flow of mercury that the effect is only to utilize the weight of this element. It is the impression of this group utilizing this tube that weight in the end of the tube causes it to be passed more readily.

The third type of tube, the simplified intestinal decompression tube (3), uses as its propulsive mechanism mercury confined within a loose balloon attached to the very tip of the tube. In this way, the loose balloon does not limit in any way the utilization of all the physical properties of the mercury. The mobility, weight, and cohesive power of this heavy metal causes it to flow freely with every change in position of the patient. As a result, the tube-head is carried readily downward into the lowest reaches of the gastro-intestinal tract by so posturing the patient that the anatomical part into which we wish the tube-head to go is always downhill until the tube head has passed the duodeno-jejunal flexure. From that point on, ambulating the patient readily results in a rapid intubation.

Many surgeons are of the opinion that making more than two holes would violate one of the simplest laws of physics. That is, that with an increase in the number of holes the negative suctioning pressure transmitted to the most distal hole would be negligible and that all the suctioning force would be exerted in the first few holes. If this premise were reduced to in-vitro experimentation, it could readily be shown that such is indeed the case and that the amount of suctioning pressure exerted by the most distal holes would be very low. By such in-vitro experimentation, then, it would seem that there would be no necessity for more than two small holes for suction. However, the error of this concept lies in trying to apply the laws of pure physics as noted in-vitro experimentation to living conditions as found in the human gastro-intestinal tract. In the human bowel we find far different conditions than were found in experiments conducted in glass or even rubber tubing. The human bowel wall being made up of two thick muscular layers one of which runs longitudinally down the gastro-intestinal tract whereas the other encircles it, tends to resist any attempt at distention. Finally when the bowel is distended the elasticity of the muscle layers continually attempts to contract down to its nondistended state. This is a fundamental act of all living muscle tissue. In addition to the positive pressure exerted upon the lumen of the bowel by the attempt at contraction of the bowel wall, we find a definite increase in intra-abdominal pressure which

Submitted March, 1949. Grace Hospital, Detroit,

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varies with the status of the patient. Briefly, it has been well demonstrated that straining at stool results in an increase in intra-abdominal pressure of over 80 cm. of water and ambulation raises the intra-abdominal pressure appreciably. When this intra-abdominal pressure is added to the pressure exerted upon the lumen of the bowel by the contracting efforts of the bowel wall, it should be quite apparent that a considerable force is exerted upon the intestinal contents forcing it into the holes of the intestinal tube regardless of their number. If now to this positive pressure forcing the intestinal contents into the holes of the tube, we remember that a negative pressure is applied to the end of the tube to suction it out, it should be quite obvious that ALL the holes must participate in the suctioning-out process. It must also be apparent that the holes must be of such a size as to permit the intestinal contents both gas and liquid being forced into the lumen of the tube with ease. The larger the holes obviously the easier the passage from the bowel into the tube. The only limitation to the size of the holes is the circumferential diameter and strength of the rubber tube.

In any tube which is being used as a decompression unit and in which intra-intestinal pressure is a major factor in forcing the intestinal contents into the tube, the greater the number of holes the more effective such a tube must be. The only limitation to the number of holes that can be used in a tube of this type is the length of the esophagus or the distance from the external nares to the cardiac end of the stomach. We have amply demonstrated that if more than eight holes are made in the tube that one or more hole will be found in the nose or naso-pharynx when the tube head comes to lie in the stomach. As a result of this, the gastric contents would shoot out through such holes soiling the bed and patient and causing much discomfort.

The observations of Galileo in 1589 that bodies of different weights fall with the same velocity can be applied in-vivo only when the mercury used in the balloon is used as a dead weight owing to the restricting effect of the shaft of the tube through the center of the balloon. Under such conditions increasing the weight of the heavy metal in the balloon would not appreciably

alter the speed of downward descent of the tube so constructed.

Observations in over three hundred cases in which a simplified intestinal tube was used with the balloon at the tip and unrestricted flow of the mercury permitted, we have been able to demonstrate that the observations of Galileo do not apply to the use of tubes in vivo. We have repeatedly demonstrated in cases of paralytic ileus the failure of intubation with the use of four c.c. of mercury and the prompt success of intubation in the same case by using eight c.c. of mercury. In such cases doubling the amount of this highly mobile heavy metal successfully intubates patients not because of the increased speed of fall but because of the markedly increased PULL exerted by a heavier mobile tube-head with the patient ambulatory. If we consider the speed of intubation as that time needed to pass a tube far down the gastro-intestinal tract, then increasing the amount of mercury in the tube-head definitely increases the speed of intubation. Thus although Galileo's observations apply with regard to free falling bodies they do not apply to bodies in vivo that must overcome the resistance of sphincters and pull a tube behind them.

### Conclusion

1. Increasing the number of holes in intestinal decompression tubes increases their efficiency because such tubes do not depend upon a negative suction pressure at the end of the tube, but rather the intestinal contents are forced into the tube by an increase in the intra-luminal intestinal pressure.

Increasing the size of the holes increases the efficiency of the tubes by making it easier for intestinal contents to enter the tube and decreases the chances of

plugging

In cases of paralytic ileus, increasing the amount of mercury in the tube-head definitely increases the speed of intubation and appreciably reduces the percentage of failures.

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# ANGINA PECTORIS SIMULATED BY CHRONIC PERIPANCREATITIS AND PANCREATITIS

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P RECORDIAL pains radiating into the left arm are segmentally considered to be signs of pathology of the coronary arteries. However, occasionally, it happens that these complaints are due to causes which are not at all related to the cardio-vascular system. Having seen such a case, we want to report it.

The patient was 48 years old, a baker, who had enjoyed good health up to two and a half years ago.

\*The Surgical department of St. Clare's Hospital, New

York City. Submitted March 22, 1949.

Since that time, he started to have pains in the pit of the stomach. His attending physician considered his complaints to be due to gas and treated him accordingly, however, with no constant relief. Within the next year, the pains became stronger, now moving to the chest and radiating into the left arm and back. The diagnosis of angina pectoris was made and the patient treated accordingly. Again, the treatment brought no relief.

The pains got so bad, that the patient was unable

JANUARY, 1950

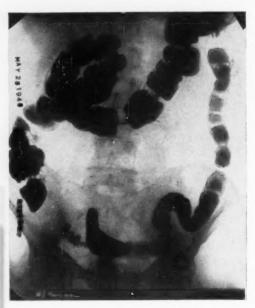


Figure 1—Peripanereatitis. Barium enema shows a loop of the hepatic flexure fixed in the midline.

to work during the last four months before being seen by us. He did not remember having had any accident. On slightest exertion, the patient had pains over the stermun. These pains radiated into the left arm and back. The weight of the patient was stationary.

The physical examination revealed a heavy-set man. The heart sounds were normal, the heart action was normal. The blood pressure was normal. The tongue was slightly coated. There was a tenderness in the epigastrium, however, no tumor could be felt. The cardiogram showed a low voltage in all ventricular complexes. It was considered to be normal. Therefore, a thorough roentgenological study of the gastro-intestinal tract was done.

The gallbladder was well visualized 15 hours, after oral Graham test. The shadow was of normal size, shape, position and density. One hour after fatty meal, the shadow had decreased 70% of its previous size. There were no signs of the presence of stones.

The roentgenological examination of the colon revealed that the gut filled with the contrast substance without delay. The rectum and sigmoid were normal. The transverse colon showed a loop formation (Fig. 1). The hepatic flexure was fixed somewhat higher and more to the midline than normal. There were no defects visible. The patient was able to evacuate only poorly at the beginning, but, after application of a glycerine suppository, he was able to evacuate satisfactorily, so that the mucosa of the colon was visualized. The mucosal pattern of the gut was normal. The hepatic flexure stayed in its fixed position. In spite of laxatives and an enema, there was still some barium in the colon two days after the first examination.

The oral administration of the barium passed the esophagus without delay and filled the stomach immediately. The mucosal folds of the stomach were normal. The organ showed hookform, was of normal size and position. The walls were pliable. The curvatures were normal. The peristalsis was active. The pylorus opened without delay.

The duodenal cap was triangular and normal. The duodenal loop was enlarged and showed external pressure effect on its concavity. The mucosal folds were normal. (Fig. 2). There was no delay in the passage of the contrast medium. The small intestines were normal in outline. The stomach was empty at the 2 hour examination, and the loops of the ileum, cecum, and transverse colon were filled. The roentgenological appearance was that of a tumor of the pancreas without invasion of the gastrointestinal tract. It was considered to be a benign process, possibly a cyst of the pancreas.

OPERATION PERFORMED UNDER GENERAL ANESTHESIA June 4, 1946

Midline incision was made between umbilicus and xyphoid process. Peritoneum was opened, no adhesions to the parietal peritoneum were encountered. There was a solid layer of adhesions from a fold of the gastrocolic ligament and omentum with the transverse colon and small intestines. Part of the omentum covered the gastrocolic ligament and major curvature of the stomach and transverse colon. The stomach, therefore, seemed to be pulled down against the transverse colon. Part of the omentum was found adherent to the cecum and ascending colon. This part



Figure 2—Peripanereatitis. The stomach shows extrinsic pressure in the antral region and a widened duodenal loop. Film taken in erect position shows the fluid levels in the colon and its abnormal position,

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of the adhesions caused tension between the transverse colon and cecum. The omentum was freed by sharp and blunt dissection. It was definitely thickened in its lower part, the fatty granules being very marked and showing grayish discoloration. The underlying structures now became visible-stomach, gallbladder, and duodenum were found normal. The head of the pancreas was felt definitely thickened; it did not feel hard, but rather like an inflammatory swelling. After separation of the gastrocolic ligament, a condition of chronic peripancreatitis and pancreatitis was found to be present. Capsule of pancreas was also thickened and no pus or old scar formation was seen. A cigarette drain was placed beneath capsule of the pancreas, the abdomen was closed in 3 layers and clips applied to skin. Cigarette drain was removed after 48 hours. The postoperative course was uneventful. Since the operation, the patient feels fine. The angina pectoris-like pains have disappeared. Frequent re-examinations have showed that the patient is in good health and working.

### Discussion

Pains in the region of the heart, radiating into the left arm, are frequently a diagnostic puzzle. Of course, the first thought in such cases, is that of a cardio-vascular condition. In the reported case, however, neither the physical examination, nor the cardiogram, nor the result of the therapy, enabled us to come to a definite diagnosis. Especially, the failure of relief of the pairs after administering nitroglycerin, is a sign, in the absence of heart failure, that we are dealing with a condition which only simulates an attack of angina pectoris.

The literature contains many reports in this respect, however, as far as it is known to us, we did not find that chronic peripancreatitis and pancreatitis, could cause such symptoms. In the reported case, we excluded at first, the gallbladder as the cause of the symptoms.

Our second idea was that a partial obstruction of the large intestines could be present, which could be ruled out after the barium enema. However, the high fixation of the hepatic flexure with shift towards the midline, was a striking abnormal feature. The fluid levels in the cecum, seen in erect position two days after the first examination (Fig. 2) made us think of a peritoneal irritation in the absence of a definite obstruction. It became apparent now, that the hepatic flexure was lying close to the duodenum. The duodenum showed definite effects from extraintestinal pressure, so that a definite diagnosis of a mass in the region of the puncreas was made. These findings were so obvious that surgery could be advised.

This case emphasizes the importance of very thorough studies of the gastro-intestinal tract in cases in which patients with angina symptoms do not respond to therapy and in which the diagnosis cannot be supported by the necessary cardiological examination. We want to stress the symptom of the displacement of the hepatic flexure towards the midline and upwards, for, we had the opportunity to see similar displacements in cases of pathology of the pancreas. However, as these cases have not been large in number, and not thoroughly studied, we want to draw the attention to this symptom, in order to have it studied by other workers.

### SUMMARY

The case of a patient is described whose complaints were those seen in angina pectoris. The cardiogram was negative. There was no improvement after the routine treatment for angina pectoris. The roentgenological examination revealed a mass in the region of the pancreas towards the right side of the transverse colon with adhesions. The operation revealed a chronic peripancreatitis and chronic pancreatitis. There was an induration of the pancreas. The adhesions were lissected. After the operation the patient was relieved of his pains which simulated angina pectoris.

# MASSIVE RESECTION OF THE SMALL BOWEL FOR ADENOCARCINOMA OF THE JEJUNUM\*

ROBERT J. KOSITCHEK, M.D. AND MARCUS H. RABWIN, M.D., F.A.C.S., BEVERLY HILLS, CALIFORNIA.

M ASSIVE resection of the small bowel is defined in the literature as the removal of 200 cms. or more, representing almost one-third of the average length of the small intestine. As a result of experimental work published by Senn in 1888, it was thought for many years that this represented the limit of safety. In recent years, however, with improved methods of coping with nutritional problems, considerable interest has been built up in the extent to which excision of the lowel may be carried. The literature is steadily accumulating reports of cases in which large portions of small intestine have been extirpated with recovery, but in each instance only the amount of bowel taken out is stressed, where-

as it is our contention that the length of bowel remaining in the abdomen is obviously the most important consideration.

A case of regional ileitis was reported by Todd in 1940, in which after five operations, there remained only three feet of small intestine. This is the smallest amount of remaining bowel which was recorded.

In the case we are presenting, the entire small intestine, except for eight inches of terminal fleum, was extirpated in order to eradicate the lesion. However, the specimen removed measured only 86 inches or 215 cms., indicating that the patient had only eight feet of small intestine to begin with. Bryant, in 1924, reported in studies of 1161 observations in which the average length of small intestine was 21 feet, 6 inches, the shortest bowel observed being 10 feet and the longest 40

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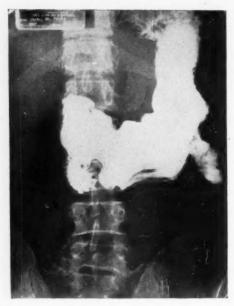


Figure 1. Pre-operative upper gastro-intestinal film revealing complete obstruction to the flow of barium in the first part of the jejunum with abdominal pressure on palpable tumor mass.

feet. Our patient had an exceptionally short small howel.

Haymond in 1935, collected from the literature 257 cases of massive resection. The results depended on the amount of bowel removed and the nature of the disease necessitating the surgery. Immediate mortality in the reported cases was about 30%, but it must be remembered that cases with recovery are much more apt to be reported so that the actual mortality is probably considerably higher.

The conditions for which massive resections were undertaken most commonly were volvulus, intuss isception, strangulated hernia, mesenteric thrombosis, abdominal injuries, tumors of the bowel involving the mesentery, and tuberculosis.

In analyzing the end results, Haymond concludes that one-third of the small intestine can be resected with a complete return of normal function. Fifty percent removal constitutes the upper limit of safety, and above fifty percent the end results may be poor, although in occasional instances the functional recovery may be better than predicted. In our case approximately 90% of the small intestine was removed.

Inasmuch as the lesion involved in our case was adenocarcinoma of the jejumun, we would like to present briefly the important features of this relatively rare disease. The incidence can be judged by a report from the Mayo Clinic indicating that between 1907 and 1939, 83 cases of carcinoma of the jejumum and

ileum were observed. An accurate pre-operative diagnosis was made in a very small percentage of the cases, but an analysis of the histories indicated that in 80% of the cases, the outstanding features were recurrent attacks of intestinal obstruction with intercurrent relief, and anemia with weakness and fatigability. If the lesion is suspected, careful small bowel X-ray observation may establish the diagnosis of small bowel tumor.

In 80% of the cases of malignancy of the small lowel, the tumor is adenocarcinoma. The treatment is resection with primary anastomosis, but the end results are poor because of delayed diagnosis in most cases.

CASE REPORT: Mr. J. B. a 52 year old white male, first consulted one of us (RJK) on January 21, 1946. Chief complaints at that time were loss of weight and ease of fatigue. The present illness dated back to March, 1943, at which time he had a feeling of nausea followed by vomiting; the vomitus containing the breakfast which he had ingested two hours previously. He consulted his local physician who ordered X-ray studies of his stomach and lower howel, which revealed no abnormalities. In August 1943, the patient had again a vomiting spell and consulted a physician, who, reportedly, told him his Wassermann and blood count were normal but offered no explanation for the symptoms. In February, 1944, while taking his wife to see her physician, he had a blood count done by the physician who told him that his hemoglobin was approximately 60% of normal and advised him to take treatment for the anemia. This he did until August of 1944, and the patient maintains that he felt fine following a series of intensive intramuscular injections. In September, 1944, the patient found that he had lost 24 pounds of weight and was



Figure 2. Post-operative upper gastro-intestinal x-ray demonstrating barium flow through anastomosis and the short distance between pyloric antrum and ileocecal valve.

unable to hold any food on his stomach. He was again subjected to X-ray examination which was negative and he was advised to see a nerve specialist. In October, 1944, he had his tonsils removed, following which he felt better and gained back all of the weight he had previously lost.

The patient felt well until the spring of 1945 at which time he again became very anemic and again took a series of intransucular injections until July of that year, when he moved from New York to Los Angeles. In September, 1945, he complained of rarked weakness, was unable to walk more than half a block vithout dyspnea. He again consulted a physician who treated him for anemia. The anemia showed some improvement until November, 1945 and again the symptoms returned. Early in January, 1946. Further X-ray studies were also negative.

On January 21, 1946, the patient consulted one of us (RJK) complaining of extreme fatigue and inability to carry on his work of shoe repairing. He complained of occasional cramplike pains in the upper abdomen associated with periodic attacks of nausea and vomiting. There was no history of hematemesis, diarrhea, or melena. There was a weight loss of about 30 pounds in the last six months. Except for his present illness his previous general health had always been good.

Physical examination revealed a thin, somewhat emaciated white male, of sallow complexion, 5 ft. 6 in, tall, weight 103 pounds, who appeared to be chronically ill. Blood pressure, 110/60, pulse 70, respiration 18, temperature 98.4. The skin was dry, icteric, and showed evidence of recent weight loss. The heart was normal in size and there was a loud, blowing systolic murmur heard all over the precordium. A2 was equal to P2. The abdomen was scaphoid in type. The liver, kidneys, and spleen were not palpable. A lemon-sized tumor mass could be palpated to the left of the umbilicus. The mass was somewhat movable and tender to pressure. Peristalsis was active. Examinations of the genitalia, rectum and prostate gland were normal. No masses were felt by digital examination of the rectum or seen by proctoscopic examination. The extremities were thin and the reflexes were normal throughout.

Blood studies on January 21, 1946, revealed 25% hemoglobin, 2 160,000 red blood cells per cubic centimeter, white cells numbered 4,450 per cubic centimeter, with 81% polymorphoneutrophils, 13% lymphocytes. Schilling count revealed basophiles 2%, eosinophils, 1%, myelocytes 3%, juvenile cells 3%, stab cells 18% monocytes 3%. The red blood cells showed

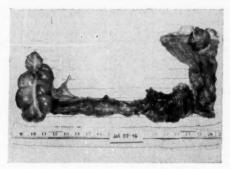


Figure 3. Post-mortem specimen demonstrating stomach and all that remains of the small intestine and caecum.

poikylocytosis and anisocytosis. Pessary cells were also present. The sedimentation rate was 25 mm, per hour, normal in males being up to 18 mm, per hour. Wassermann and Kline serological tests were negative. Icterus index was 4.2. Urinalysis was essentially negative. Blood calcium was 9 mgms.%, blood posphorus was 2.2 mgm.%, alkaline phosphatase was

2.9 (Bodansky units.) Platelets were 136,000 per ec.; coagulation time (by the method of Lee and White) 6 minutes; bleeding time 3 minutes. Gastrie analysis revealed no free hydrochloric acid in the fasting specimen, but subsequent specimens taken at 15 minute intervals showed a normal percentage of free



Figure 4. Post-mortem section of liver studded with metastatic carcinomatous implants.

hydrochlorie acid. There was no lactic acid or occult blood; there were a few pus cells and a moderate number of bacteria and a moderate amount of meus. Blood sugar 117; prothrombin time 8. Serum protein 9.15 grams with an albumin of 5.18, globulin 3.97 gms, with an albumin-globulin ratio of 1:1.3.

Stool examination on January 21, 1946, revealed no occult blood. Stool examination repeated on January 29, 1946, showed 4 plus blood in two different specimens. Blood amylase was normal. Examination of material obtained by stranger of the stool of the stool of the stool of the stool travenous urography revealed no abnormalities.

Gastro-intestinal X-ray revealed a medium sized fish-hook type of stomach with no evidence of herniation or cardiospasm. The mucosal pattern study and peristalsis were normal and no filling defects were seen. The pylorus and duodenal cap were smooth and regular in outline. Serial films were taken in various projections all of which showed a normal stomach and duodenal cap. However, considerable spasticity was observed in the first portion of the jejunum with a narrowing shown in one of the films with a moderate dilatation of the bowel in the region corresponding to the mass palpated clinically. Four hour observation showed a fairly normal progress of the barium, the head of the barium column being at the ceeum. However, there was retention of the barium in the upper small bowel. The twenty-four hour observation showed a normal progress of barium scattered from ceeum to rectum.

A diagnosis was made of tumor of the jejunum based on X-ray evidence of partial obstruction in this area associated with severe anemia and gastro-intestinal bleeding. In view of the four years history, the lesion was considered benign.

The patient was prepared for surgery with one whole blood transfusion and 10 units of red blood cells over a period of two weeks. Operation was performed by one of us (MHR) on February 11, 1946.

An annular carcinoma of the first portion of the jejunum was found completely obstructing the small bowel. There was extensive glandular involvement in the mesentary of the jejunum, forming a large carcinomatous mass completely surrounding the superior mesenteric artery and vein. There was marked dilatation of the jejunum and duodenum, proximal to the obstructing lesion.

Inasmuch as the patient had been bleeding severely and inasmuch as the lesion was completely obstructing the bowel, it was decided that radical excision with sacrifice of the superior mesenteric vessels was indicated and justified. The third portion of the duodenum was mobilized and the superior mesenteric vessels cut across above the lesion and doubly tied with chromic catgut. The duodenum was freed and cut across approximately 3" proximal to its junction with the duodenum. The entire lesion consisting of the tumor together with the large mass of mesenteric glands was mobilized and removed en bloc.

It was found that the eecum and terminal ilcum were viable but it was necessary to resect the entire small bowel within 8 inches of the ileo-cecal junction. The open end of the terminal ilcum was closed with a running suture and reinforced with a purse-string of catgut, further closure reinforced with several mattress sutures of fine silk. An end to side anastomosis of the open end of what was left of the third portion of the duodenum to the side of the ilcum was then carried out using a running suture of fine intestinal catgut uture reinforced by a layer of interrupted silk. The anastomosis admitted two fingers when completed. 100,000 units of Penicillin was left in the peritoneal cavity. The abdomen was closed without drainage using continuous chronic in the peritoneum and posterior rectus fascia; interrupted chronic in the muscle and anterior rectus fascia; interrupted dermal for the skin. The patient received 1500 cc of blood during the course of the procedure and left the operating room in excellent condition. The immediate post-operative course was relatively uneventful.

The case provided us with an interesting physiological study. It has been well established that food absorption is practically confined to the small intestine, absorption from the large intestine being confined to water and inorganic salts.

It has been estimated that the absorption area of the small intestine is about 10 square meters. In our case we estimate that 1 square meter of absorption surface remained intact.

The digestive processes which are carried out in the small intestine are quite capable of rendering ordinary foodstuffs cuitable for absorption without the assistance of gastric enzymes. The enzymes which are responsible for digestion are secreted by the panereas and the glands in the mucous membrane of the small intestine.

Following recovery from the operation, the patient presented a challenge in nutritional management. began to have 8 to 10 light colored, semi-liquid, foul on the fourth post-operative day. The total fat exceeded 30% of the dried stool, 76% of which was hydrolyzed. Fat metabolism was regulated by a low fat diet, and the administration of Evidently an internal secretion of the pancreas pancreatin. Evidently an internal secretion of the pancreas is concerned in some way with fat metabolism since the fatty liver which follows pancreatectomy in the experimental animal kept alive with insulin can be avoided by the administration of lipocaic or raw pancreas. A cortical hormone was given to increase phosphorylation and thus increase delayed fat absorption. Bile salts were given. The calcium deficiency, so often seen in steatorrhea, due to either lack of absorption from the intestine or excessive re-excretion of the calcium into the intestines was controlled by feeding large doses of calcium and Vitamin D. The vitamin deficiency was treated with parenteral injections of vitamins and crude liver extract.

Protein metabolism requirements were met with a diet containing 400 grams of protein daily and four hourly feedings of a tablespoonful of protein hydrolysate.\*

Fermentation was taken care of with 600 grams of earbohydrate. Fermentative action was brought about with the help of acidophilus milk. The ingested organisms through their action on earbohydrates produce organic acids, acetic butyric and lactic acid.

Tineture of belladonna was given to reduce the tonicity of the musculature of the small bowel and allow more time for absorption,

The patient showed steady improvement by a gain of twelve pounds in weight and steady gain in strength which enabled him to be up and about. He averaged about three light brown, semisolid stools daily. On June 4, 1946, the patient was taken into the Clinic at the Cedars of Lebanon Hospital for purposes of more closely studying the chemical and digestive mechanisms associated with such a large resection of the small bowel.

The following are the laboratory reports obtained through the courtesy of this Clinic; The blood count on June 4, 1946 showed a hemoglobin of 80%. The red blood count was 4,500,000 per cc. and the white blood count was 5,100 per cc. with a normal differential. The sedimentation rate was increased for the first time since surgery, 12 mm in 52 minutes (Westergren). The stool was foamy and not well formed with occasional meat fibers and neutral fat globules. No fat, ameobic cysts or parasites were seen. The alkaline phosphatase (Bodansky) was 17 units. Serum calcium was 10.9 and blood phosphorous 2.4. On June 21, a four hour glucose tolerance test performed by oral ingestion of 100 grams of glucose gave the following results:

TIME	URINE FOR SUGAR	BL. SUGAR IN MGM. %
Fasting	Negative	83
½ hour	Negative	103
1 hour	Negative	113
2 hours	Negative	115
3 hours	Negative	98
4 hours	Negative	84

A 24 hour stool analysis:

- A-Moisture based on wet stool-91.36%
- B—Weight of dry stool (residue)—8.64 gms, based on  $100~\mathrm{gm}_{\star}$
- C-Total fat 16% of dry stool
- D-Fatty acid 13.9% of free fat
- E-Fatty acid in fat fraction-87.3% of total fat.
- F-Nitrogen-2.48 gms, in 240 hours (normal-1-2 gms.)

The oral hippuric acid test expressed as sodium benzoate was 0.9 grams in four hours (normal values—3.5-4.0 gms.)

On June 26, it was noted that the patient was becoming edematous. There was pitting edema of the ankles and legs and a fluid wave was felt over the abdomen associated with shifting dullness in both flanks. The blood count showed a drop in hemoglobin to 73% and the red blood count to 3,920,000 per ec. Total serum protein was 6 grams. Electrocardiographic studies revealed diminished myocardial tone with low voltage QRS complexes and low voltage T waves. An attempt was made to do circulation times and venous pressure, but it was impossible to get into the patient's veins. The patient suddenly expired on July 2, 1946.

Post-mortem studies were perfomed by the pathologist of the Cedars of Lebanon Hospital. The gross external description reveals an emaciated but otherwise normal proportioned white male appearing younger than the stated age of 53. Five feet four inches in height and weighing 84 pounds. There was a well-headed abdominal wound.. A purpuric cruption was noted over the hands and face. There was a marked, virtually complete, absence of sub-cutaneous fat.

Pertinent gross autopsy findings: The cardiovascular system 84 pounds. There was a well-healed abdominal wound. A striking degree of serous atrophy of the subepicardial fat was noted. The heart weighed 280 gms. The valve circumference measurements were normal. The myocardium was diffusely brown and showed no gross sear or other lesions. The coronary arteries were patent and showed no gross selerosis.

The respiratory system grossly revealed 50 cc. of clear colorless fluid in the right and left pleural cavity. Repeated surfaces were crepitant and showed increased hyperemia.

The peritoneal cavity contained 700 cc, of clear fluid. The duodenum anastomosed to the terminal ileum through what appeared to be an intact base of mesentery. The anastomosis was located in the second portion of the duodenum just distal to the ampulla. The anastomosis its appeared well healed, the stoma widely patent. The length of the duodenum from the pylorus to the site of the anastomosis was 20 cm, and this organ did not appear unusually large or dilated. The length of the remaining ileum from the anastomosis to the ileo cecal valve was 23 cm. This portion of terminal ileum shows no gross lesions. The large bowel shows no lesions and no evidence of tumor. There was no evidence of residual tumor at the site of anastomosis, but the adjacent mesentery

<sup>\*</sup>Prominegen (Person and Covey),

contains a sizable firm, yellow-gray tumor mass, perhaps 6 cm. in diameter which resembled regional nodes, although nodular character of lymph nodes was not apparent. The pancreas was of normal size and on repeated section showed no gross lesions.

The liver weighed 1500 grams. The edge protruded just to the costal border. The external surface, particularly of the right lobe, was studded with numerous slightly elevated tumor nodules. These tended to be of moderate size, ranging from 1 to 3 cm. in diameter. Cut surface of the liver showed marked replacement of parenchyma, particularly in the right lobe, by tumor nodules varying up to several centimeters in diameter. The nodules were generally well-preserved, yellow-gray, and showed central zones of necrosis. The parenchyma, apart from being compressed and replaced by tumor, was not remarkable. It was generally dull brown in color and did not show bile staining.

The lymphatic system was remarkable in the fact that there was a lymph node involvement behind the site of the anastomosis, as above described, and involvement of the lymph nodes in the left retroperitoneal area. The gall bladder, biliary tract, spleen, urinary system, genital system and endocrine system were not remarkable.

The microscopic post-mortem studies: The section of the adrenal gland showed a narrow zona glomerulosa with small cells. The fascicular layer was correspondingly prominent and contained a moderate amount of liquid.

The pituitary gland was characterized by an irregular nodular zone within the anterior lobe in which there appeared to be degenerative changes in the form of loss of extuplasmic staining together with nuclear distortion. This zone was interpreted as an area of degenerative change rather than a microscopic adenoma, with "exhaustion" of activity.

Sections of skin showed atrophy of the epidermis associated with dermal clastosis of senile type. In addition there was an area of recent hemorrhage corresponding to the gross purpura noted. This was not associated with tumor infiltration or other recognizable change.

The sections of the liver were partially occupied by metastatic tumor. The tumor was of an irregular alveolar adenocarcinoma pattern. In some areas the alveolar pattern was well preserved; in others the growth was rather anaplastic. There was a loose, moderately vascular, fibrous stroma, at times containing degenerated tumor cells. There was evidence of nucinous secretions both within the lumen of the tumor alveoli as well as with the cytoplasm of many of the tumor cells. The somewhat compressed adjacent liver parenchyma showed simple atrophy and fragmentations of cell cords, some nuclear attypism and focal collections of bile, apparently within dilated canaliculi. A block of liver apart from the metastatic nodules showed moderately simple atrophy associated with some disorganization of cell cords. In addition there was frequent prominence of bile canaliculi and some bile staining of liver cells. This was most prominent in the center portion of the lobules. In many areas there appeared to be sinusoidal hyperemia or at least the sinusoids are prominent in relation to the shranken liver cells. For the most part fatty changes were notably absent in the liver cells.

The kidneys showed essentially normal architecture. Some of the convoluted tubules showed severe cloudy swelling. Crystals morphologically compatible with sulfonamide crystals were noted in some of the collecting tubules.

Lymph gland sections taken from contiguous areas show tumor cells similar to that seen in the liver.

The pancreas was characterized by normal acinar ductal structure. By contrast, the islets showed some abnormality in that all stood out with unusual clarity from the surrounding

pancreatic parenchyma as the sult of disappearance of much of the cytoplasm of the islet cells, so that in many of the islets the cells were characterized by virtually bare and frequently hyperchromatic neclei. In other areas, and in most of the islets, sections showed histologic appearance.

### SUMMARY

A case of carcinoma of the jejunum is presented which escaped recognition for four years. Radical resection was performed because of obstruction and profuse bleeding into the bowels, necessitating removal of all of the small intestine except for eight inches of terminal ileum. A satisfactory nutritional status was attempted by careful medical management for a period of six months at which time death occurred as a result of extensive liver metastases and hepatic insufficiency. Had this operation been done for a benign lesion, we feel that the patient could have been maintained in fair health indefinitely despite the small portion of small intestine remaining, thus offering encouragement to perform massive resection when indicated in the presence of extensive mesenteric trauma, volvulus, intussusception, regional enteritis, small intestinal tumors, and other conditions in which the major portion of the small bowel is devitalized by disease or injury.

### Conclusions

- 1) A case is presented in which 90% of the small bowel is resected for primary adenocarcinoma of the jejunum.
- 2) Patient surviving for six months after massive resection of the small bowel and finally succumbing to metastatic carcinoma of the liver.
- The implication that massive resection of the small bowel is compatible with life under adequate medical care.

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# ADSORPTION OF BACTERIAL TOXINS BY INERT PARTICULATE MATERIALS

JACK MOSS AND GUSTAV J. MARTIN, Sc. D. PHILADELPHIA, PA.

Logic indicates the ideal intestinal adsorbent would possess: 1. Maximum capacity for the inhibition of lysozyme. 2. Maximum capacity for the removal of toxic amines, tyramine, histamine, putrescine, cadaverine. 3. Maximum capacity for the removal of toxic bacterial metabolites such as indole and skatole. 4. Maximum capacity for the removal of toxic substances of unknown nature produced by bacteria. 5. Maximum capacity for the removal of agents such as paralytic shellfish poison. 6. Absence of any tendency to remove essential food factors, e.g. vitamins, minerals, amino acids. 7. Non-toxicity. 8. Patient acceptability.

The present report deals with the capacity of various adsorption and ion exchange materials to remove toxic substances of undefined nature from lysed bacterial preparations. While there are many clearly defined toxic elements produced by bacterial metabolism such as histamine, tyramine, putrescine, cadaverine, indole, skatole, etc., there is an even larger number of substances of unknown chemical composition with high

Research Laboratories, The National Drug Company, Philadelphia, Pa. Submitted June 30, 1949.

toxicity elaborated by bacteria. It is possible that these chemicals play a role of etiological significance in the degenerative diseases.

### EXPERIMENTAL

### Cultures

(a) Shigella dysenteriae no. 758 National Institute of Health, (b) Eberthella typhosa—FSBA no. 3249, (c) Escherichia Coli—no. 8739—A.T.C.C.

### Toxin Production

The toxins (or toxic material) of the above organisms were prepared according to a modification of the method described by Branham and Habel (1). The organisms were cultivated on Difco Brain-Heart Infusion Agar.

### Treatment of Toxins

The various adsorbents were added to the toxins to give a final concentration of 10 mg. per ml. (The synthetic zeolite was also tested at 20 mg. per ml.) The mixtures were shaken at room or incubator temperatures for two hours; then centrifuged and titrated

TABLE I Adsorption of Toxic Substances from Bacterial Lysates

	Approximate MLD per ML					
ADSORBENT	Shigella dysenteriae (shiga)		Eberthella typhosa	Escherichia coli		
Aluminum hydroxide (powdered)		50	>10	12		
Bentonite	0.5-1		0-1	0		
Veg. Charcoal	>40		0	0		
Carboxylic cation exchange Resin	<10		0,5-1	1		
Kaolin	20		12		5	
Hydrated Sodium aluminum silicate (a synthetic zeolite) 10 mg./ce.		50	1	1.3		
Hydrated Sodium aluminum silicate (a synthetic zeolite) 20 mg./cc.		50	1	5		
Synthetic zeolite 5% + polyamine resin 5%		50	0-1	10		
Synthetic zeolite 10% + Polyamine resin 10%		50	0.5	>5.		
Polyamine Anion Exchange Resin		>50	10	5		
Silien	>40		2	0		
Magnesium Aluminum Silicate		< 50	10	10		
Toxin Controls	40	50	10-12	10-12	24	

that same day or stored at 8°C. Suitable controls for each toxin were treated in a similar manner.

### Titration of Toxins

Serial 2-fold dilutions of the treated and untreated toxins were made in saline-peptone broth. Mice, at least five weeks of age were then injected intravenously with 0.5 cc of the toxin; 6 mice per dilution. The mice were observed for a period of seven days, during which the number of deaths was recorded. The approximate MLD (to the nearest whole number) was then recorded. (See Table). Repeat titrations were carried out in order to obtain an average MLD value. In most cases, the results did not vary any more than

### RESULTS

As shown in Table I, aluminum hydroxide and magnesium aluminum silicate were inactive against all three toxins.

Bentonite and carboxylic resin, were active against all three agents.

E. typhosa toxin was adsorbed or almost completely "inactivated" by charcoal, sodium aluminum silicate, silica, and a mixture of sodium aluminum silicate plus a polyamine resin. This combination was slightly more effective than either of the single agents. The toxic material from E coli was adsorbed by charcoal, hydrated aluminum silicate, polyamine resin, and silica. Bentonite, carboxylic cation exchange resin and Kaolin were the only adsorbents active for shiga toxin.

### DISCUSSION

Two types of studies have been conducted with adsorption agents and bacteria or their toxic metabolic products. First, studies designed to demonstrate the removal of bacterial cells by adsorbing agents. Such studies have demonstrated the apparent adsorption of Escherichia coli, Clostridium welchii and Lactobacillus acidophilus on kaolin, calcium carbonate, aluminum hydroxide and barium sulfate in vitro (2) Staph, aureus, Sarcina lutea and Bacillus subtilis were removed by kaolin, while charcoal removed only the staphylococci. These authors were not of the opinion that alteration in bacterial flora of the gut following the clinical use of kaolin or charcoal was due to removal of bacterial cells. Smith (3) reported the effectiveness of kaolin-alumina mixtures in adsorbing fecal material. These studies were conducted in vitro and were not interpreted as necessarily reflecting in vivo results. Similar studies (4,5,6) demonstrated the capacity of particulate adsorption agents to remove bacteria or viruses; however, it seems hardly probable that this adsorption of the intact bacterial cells plays any significant role in the clinical effectiveness of these agents. The enormous numbers of bacteria in fecal material make it virtually impossible.

Second, studies of the removal of toxins and toxic chemicals of bacterial metabolism have been made by numerous investigators. Thus, the removal by charcoal of tetanus toxin (9, 11), of dysentery toxin (6, 7, 9), of diphtheria toxin (9); by kaolin of Vib. cholera toxins (8, 12), or dysentery toxins (8), of B. enteritis toxin (8), of diphtheria toxin (8), of botulinus toxin

(8), and of typhoid toxins (8), and by aluminum hydroxide of diphtheria toxin (10).

The studies here reported cover the adsorption of toxic substances produced by Shigella dysenteriae, Eberthella typhosa and Escherichia coli which organisms commonly occur in the gastrointestinal tract and doubtless produce at least a part of their pathological effects by virtue of the elaboration of toxic chemicals. The adsorption agents studied have been previously tested for their capacity to inhibit pepsin (13), inhibit lysozyme (14), remove toxic chemicals of endogenous bacterial origin but of known composition (15) and to adsorb paralytic shellfish poisons (16). It is felt that this series of studies will permit the selection of the most logical compositions for clinical trial.

The necessity for the use of multiple adsorption agents becomes clear; no single adsorption agent possesses optimal capacity in the various systems studied. It is further apparent that if in vitro studies can be correlated with clinical results, the currently used adsorption agents are not the best of the available materials; thus, kaolin has no effect in inactivating lysozyme (14), it will not adsorb paralytic shellfish poison (16), it is not an effective adsorbent for chemicals of endogenous origin of known chemical nature (15) and in the presently reported experiments, it has been demonstrated that it does not remove the toxic substances produced by Eberthella typhosa and is only weakly active against those of Shigella dysenteriae.

### SUMMARY

Nine different adsorption agents have been tested for their capacity to remove in vitro the toxic chemicals elaborated by cultures of Shigella dysenteriae, Eberthella typhosa and Escherichia coli. The significance of the findings relative to clinical application of adsorption agents is discussed.

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# NUTRITION

### PROBLEMS IN THE INTRAVENOUS ADMINISTRATION OF SYNTHETIC AND NATURAL FATS FOR NUTRITIONAL PURPOSES

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W HEN patients are unable to take food by mouth difficulty is encountered in providing caloric intake adequate for the maintenance of nitrogen balance. The intravenous administration of fats would, therefore, be of value. It is the purpose of this paper to discuss the problems encountered in making nontoxic, stable fat emulsions of nutritional value.

The fat droplets in an emulsion are held apart by electrostatic charges on their surfaces; however, they are constantly attracted to each other by the gravitational force between two bodies. In addition, a great disparity in density between the fluid medium and the fat will increase the velocity with which the particles will rise or "cream." If these velocities are sufficiently great, the mechanical forces will overcome the electrostatic forces and the emulsion will "break." The rate of ascent is directly proportional to the size of the spheroids, the larger ones rising faster. Increased viscosity of the aqueous phase slows down the rate of ascent. These creaming relationships are expressed in the usual form of Stokes law:

V = 2G(D3 - D2)R2

Where-

V = Velocity of ascent of fat globules

G = gravitational force

Ds = density of aqueous medium Df = density of fat

R = radius of fat globules
N = coefficient of viscosity of aqueous medium,

Since the chance for a collision between two globules is proportional to the distance between them and the number of particles present, more concentrated emulsions have a greater tendency to break.

The factors, therefore, that affect emulsion stability are electrostatic charge, concentration of emulsoid, gravity, difference in density between fat and aqueous phases, viscosity of the aqueous phase and particle size. Electrostatic charge and gravitational force cannot be

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altered. The concentration of the emulsion is not subject to variation since a very dilute emulsion will have little advantage over glucose. The density difterences between the two phases should be kept as small as possible. Therefore, only the viscosity of the aqueous phases and the particle size can be effectively changed to produce greater emulsion stability. Gelatin, a protective colloid, increases the viscosity of the aqueous phase, but it is toxic (1). For these reasons, particle size becomes the limiting factor in emulsion stability.

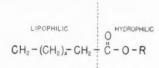


Fig. I-The molecular configuration of a common type of surface active agent derived from fatty acids is illustrated. The long chain hydrocarbon is lipophilic while the carboxyl group is esterified to a hydrophilic group.

Because the interfacial tension between water and natural fats is so great, it is difficult to prepare oil in water emulsions of sufficiently small particle size with known pressure homogenizers. It is logical that those who have worked with intravenous fats have added emulsifying agents which lower surface tension. The chemical constitution of these substances is such that one end of the molecule is fat soluble while the other is water soluble, Fig. I. The most frequently used surface lowering substance has been lecithin, (2, 3, 4, 5, 7). Emulsions prepared with lecithin have a tendency to produce anemia by destruction of red blood cells, (5, 6) plus those pathological alterations which hemolysis entails. This cellular destruction also leads to abnormal nitrogen losses.

We have prepared emulsions of synthetic and natural fats with aim of studying their toxic effects. Lethal doses, mechanisms of death, hemolytic properties, emulsion stability in vivo and in vitro, and surface active properties, all have been investigated.

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### MATERIALS AND METHODS

The surface active synthetic fats used in the present study were fatty acid esters of polyhydric alcohols; namely, spans and tweens (Nos. \*20, 60 and 80) and glucose monolaurate. Butyric acid\*\* which is a synthetic fatty acid is not considered to be markedly surface active.

Emulsions of the various fats in  $2\frac{1}{2}\%$  - 5% glucose solution were made both with and without emulsifying agents in a high pressure homogenizer. \*\*\*Tweens and asolectin are relatively water soluble and require no smalls fication.

Emulsions of natural fats were prepared without emulsifying agents by a combination of chemical and mechanical means. Corn oil to which 20% acetone had been added was emulsified in 2½% aqueous glucose solution containing 7% acetone. The acetone was then allowed to evaporate or was removed by vacuum distillation. Removal of acetone caused a partial breaking of the emulsion, especially with vacuum distillation. The resultant mixture was separated by centrifiguation or by standing. The cream and oil fractions were discarded. Although these emulsions were prepared so that the final product would contain 20% corn oil, much of the oil separated out. The end result rarely contained over 5% fat.

Relative surface tension was measured by counting the number of drops in a cc falling from the same capillary point burette. The weight of each drop was then calculated from the specific gravity of the material, and taken to represent the force necessary to break the surface. The results were compared to the values obtained for saline and water.

The ability of saline and plasma proteins to break the emulsions was observed in the test tube. The rate Let which emulsions were broken was best seen microscopically. A small quantity of emulsion was mixed with an excess of a serum protein solution of normal concentration.

- Hemolysis was determined by mixing saline washed red blood cells of sheep with the emulsions to form a 5% red cell suspension. The mixtures were incubated at 37° for 1 hour. The resultant mixture was broken by centrifugation and the addition of a few crystals of sodium sulfate. In almost all cases, the hemoglobin concentration in the supernate was measured by the method of Evelyn (8). Percentage of hemolysis was determined from a standard color representing a hemolized 5% red blood cell solution. In a few cases, when the emulsion was not completely broken, percentage of hemolysis was measured from the residual intact red blood cells in the centrifuge tube.

The lethal dose with rapid intravenous and intraarterial injections was estimated from the dose necessary to produce death in rabbits. Dogs were used in addition to rabbits in the case of the fatty acid esters of polyhydric alcohols (illustrated by span and tween in Chart 1).

In some cases, the animals had been previously injected with 5 mg. of Evans blue to measure capillary permeability to proteins. All animals were autopsied immediately after death and specimens taken for microscopic section in most cases.

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The effect of surface active synthetic fats on capillary permeability was studied in dogs and rabbits. Evans blue was previously injected to tag plasma albumin (9), Span 20 (sorbitan monolaurate) was injected into the femoral artery of a dog. The intensity of dye color in the injected and normal extremity was later compared

FAT ENJUSION	SURFACE TENSION	% HEMOLYSIS	CG TO PRODUCE
5% SEJECSE 15% SPAN 20	62%	PRECIPITATION	5-10
18% ASOLECTIN	31 %.	35	-
2 7% ASOLECTIN O 6% Na HPO		47	want
36% ASCLECTIN	47%	43	45
27% ASOLEGIN IN	45%	78	
THORACIG DUGT	-	0 "	-
IN TWEEN 20	58%	77	10 - 30
STORES OIL	17%	14	MORE THAN
MUDGE SE	23%	COAGULATION	

Chart I-Surface activity, hemolytic properties and lefhal doses of different materials are compared.

visually. This experiment was repeated in a similar fashion by comparing the lungs after the injection of one pulmonary artery with span 20.

### RESULTS

The synthetic surface active fats such as spans and tweens were toxic and hemolytic in direct proportion to their surface tension lowering properties (chart I). There were but minor differences between the effects of the different spans (20, 60, and 80) and tweens (20, (0 and 80)). The results with span 20 and tween 20 are illustrated as being representative of the entire group. Glucose monolaurate which was prepared by us is similar to span 20. Although not illustrated in the chart the mixture of spans and tweens seemed more lethal than either alone.

All of the various types of natural lecithins administered intravenously by Ashby were found to be toxic. The toxicity was slightly reduced by preventing exposure of the solutions to air (10). We have studied only asolectin, a soy bean phosphatide. It is toxic and hemolytic.

The hemolytic properties of all above mentioned substances to sheep cells were substantial when compared to a natural fat emulsion such as crinine thoracic duct lymph collected after a fatty meal. (Chart I),

Emulsions of natural fats not containing emulsifying agents were relatively non-toxic but these emulsions were difficult to prepare in suitably high concentrations.

The sodium salts of long chain fatty acids act as polar non-polar compounds and reduce surface tension. When carbon chains shorter than C-6 are used reduction of surface tension and hemolysis do not take place (11). In such cases the short carbon chain acts more like a chloride ion (12). For this reason, we in-

vestigated the practicability of using sodium butyrate as an infusion material. A 15% sodium butyrate solution buffered at ph 7.6 was toxic mainly because of its hypertonicity. Coagulation of red cells was observed at this concentration. In lower concentrations, the caloric value is not sufficiently great to warrant its use (Chart I).



Fig. II—The rapid intravenous injection of 23 ec of 10%. Tween 20° in Saline results in a sharp fall in blood pressure, shock, pulmonary edema and death within a few minutes.

The acute toxicity of fat emulsions with lowered surface tension was always manifested by pulmonary edema. Since the pulmonary capillary membranes are exposed to the highest concentration of the surface lowering substances after intravenous injection, their permeability was markedly altered. This fact was confirmed by capillary permeability studies using T-1824 dve as a tracer for albumin. Albumin rich fluid rapidly escaped into the alveolar spaces in all fatal cases. This was evident by the visual increase of the dye concentration in the lung tissue, and the presence of frothy blue fluid in the bronchi. Microscopic studies of these tissues showed only pulmonary edema. Death ensued in a shock like state, with marked lowering of the blood pressure secondary to a diffuse loss of fluid through capillary beds. (Fig. 11).

Since intra-arterial injections pass through the systemic circulation before reaching the pulmonary tree, they were slightly less toxic than intravenous injections. In the case of the spans and tweens, intravascular clotting was occasionally observed even though autopsy was completed shortly after death.

All the emulsions listed in Chart I, have been stable on standing for several months. Emulsions which broke on standing for shorter periods, were considered unsuitable for use and were not studied.

Stability in vitro does not imply that the emulsions will remain stable on introduction into the circulating blood. If equal volumes of serum and the emulsions were mixed and allowed to stand, all were broken at varying rates usually in the space of several hours. Electrolytes partially or completely neutralize the surface charges and cause fat emulsions to break. When our emulsions were mixed with equal volumes of physiological saline, rapid salting out of the fat occurred. The effect of plasma proteins upon emulsion stability was tested by mixing with purified solutions of ", " and " globulins, and albumin." All the globulin fractions caused coalescence of the fat droplets. These

findings were similar to those found with the cephalin cholesterol flocculation test of Hangar (13). In contradistinction to the globulins, purified albumin had a tendency to stabilize the emulsion. The rate at which emulsions were broken could best be determined by microscopic observation. Corn oil emulsion without the addition of stabilizer was the most stable with serum; agglutination of globules could seldom be seen. It is possible that this emulsion when diluted by slow injection might remain stable in vivo. Gelatin reduced the salting out effect of electrolytes, but did not abolish it. All emulsions tested have been broken at varying rates with serum or plasma. Asolectin itself which is water soluble forms a precipitate with plasma and purified globulins, but not with albumin. This substance therefore becomes a very poor stabilizer in the presence of globulins. The same is true for gelatin.

The lipoid granulomas observed in tissues by others (3, 7, 14), using supposedly non toxic emulsions are probably evidence of in vivo instability. In this study, pathological investigations of this nature have not been undertaken.

### DISCUSSION

The conflicting reports as to the toxicity (2, 3, 6, 7) and the practicability of using intravenous fats for nutritional purposes prompted the present investigation. Little study has been directed toward an explanation of the observed hemolytic reactions and acute toxicity. Most investigators have attempted to reduce toxic effects by greater purification of the lecithin emulsifying agents or by some variation in the source of the lecithin. The fundamental difficulty, however, does not lie in the chemical constitution of the emulsifying agent; but rather, in a physiochemical property inherent in all emulsifying agents, that is, the property of lowering surface tension.

The integrity of any cell depends upon its menibrane, which is composed of an oriented bimolecular layer of fatty substances, with a monomolecular layer of hydrated protein on the inside and outside (15). Emulsifying agents disrupt cell membranes by dispersing the fatty portion of the cell membrane into the surrounding aqueous medium. The surface lowering property is responsible for the efficiency of these substances as emulsifiers, and for the ability to produce disruption of cell membranes. The latter causes increased capillary permeability and hemolysis. Animals on high fat diets become anemic (16, 17), because a small portion of the fat is probably absorbed as surface active soap, rendering the thoracic duct lymph hemolytic (17).

The choice of lecithin as an emulsifying agent is a natural one since, it is, a normal constituent of human blood. Hyperlipemia in humans occurs with concentrations of phospholipid (most of which is lecithin) as high as a 2 gm per 100 cc. The serum in these cases cannot be considered hemolytic. Either the lecithin of plasma must be rendered non toxic and non hemolytic by conjugation to protein or else infused lecithins must be different because of impurities or variation in chemical composition. Since absolute purification by present chemical methods is difficult, it has been suggested that the properties of individual lecithins be ascertained by

synthesis (18). Further confusion results from the fact that natural lecithin is a mixture of both the and the <sup>β</sup> form (19). Variation in the proportions of these constituents may conceivably alter their physiological behavior. The preparation of synthetic lecithin (18, 20), might offer a solution to some of these perplexing

questions.

Contradictory observations by various authors (6, 21) as to the utilization of intravenous fat emulsions, might be accounted for on the basis of nitrogen losses secondary to hemolysis. Weight loss would naturally occur with animals on negative nitrogen balance, which would depend upon the extent of hemolysis produced by the emulsion. The establishment of a positive nitrogen balance on a low caloric diet with adequate protein after intravenous fat administration is suggested evidence for utilization of the infused fat (21). It does not exclude that the fats are hemolytic unless careful studies on blood pigment output are done.

In Vivo instability of emulsions would seem to be a contra-indication to clinical usage. When solid fats such as coconut oil are used agglutination of particles may occur without the formation of oil globules. Since such clumping is not always observed in vitro, erroneous impressions about emulsion stability may be formed. Purified globulin fractions caused the tested emulsion to break and asolectin to precipitate. In most infectious illnesses, some of the globulin fractions are elevated. In illnesses such as cirrhosis, the plasma globulin fraction may be considerably elevated. The use of present day intravenous fat emulsions for these reasons may conceivably be contraindicated in diseases where its use might be most beneficial, since it is analogous to the in vivo performance of a cephlin cholesterol flocculation test of Hangar (14). The salting out effect of electrolytes would add to the instability.

This work seems to indicate that preparation of fat emulsion suitable for intravenous use should have particle sizes unobtainable by pressure homogenizers alone. The addition of materials which lower surface tension make achievement of small particle size possible. On the other hand, the toxicity of these surface active agents make their use undesirable.

Water soluble or dispersible synthetic fats should be ideal for manufacturing stable infusion products. Synthetic fats may differ from natural fats by modifying either the fatty acid chain, or the alcohol to which the fatty acid is esterified. The unmodified fatty acid may

Fig. III-Illustrates the molecular formula of a surface active polyalcohol ester of a fatty acid. In actual practice, these derivatives are not formed as illustrated.

be combined to a quarternary ammonium ion, or to a polyhydric alcohol. Both methods would increase the water solubility or dispersability. Monoglycerides may be formed instead of triglycerides, or the fatty acid may

be combined to glucose, sorbitol or some other such compound (Fig. III). All our investigations have shown that the preparation of such water dispersible fats renders them surface active and therefore toxic. This is not the proper avenue of approach.

The work, which has been presented, showed it to be more logical to alter the fatty acid portion of a synthetic fat in such a way that the substance be free of surface tension lowering properties. We have done this by placing polar groups at varying intervals along the straight chain fatty acid in position such that the final product would not be polar-non polar and, therefore, free of surface activity. Synthetic dicarboxylic fatty acids have polar groups at both ends and do not act as polar nonpolar wetting agents (Fig. IV). We have synthesized hexadecane carboxylic acid, (COOH, (CH2)16COOH). In addition both carboxyl groups have been esterified with various groups to render the compounds water soluble,

Fig. IV-Illustrates the polar carboxyl groups at both ends of a long carbon chain. configuration renders the dicarboxylic fatty acids non surface

Our studies on these non-surface active, water soluble, substances show great promise, and will be published separately. The present communication has been limited to the background work which suggested the theoretical basis for this attack.

At the present moment, it seems to the authors that the problems in the administration of intravenous fats would be best circumvented by synthetic fat compounds which by virtue of water solubility need not be given in the usual emulsion form. Such compounds may fulfill the requirements for a high energy fat like substance suitable for infusion purposes.

### SUMMARY AND CONCLUSION

Due to the high interfacial tension between water and natural fats it is almost impossible to produce stable emulsions of these substances by mechanical means. It was found that the addition of emulsifying agents which lower surface tension, make possible the formation of stable emulsions. These emulsifying agents were found to be toxic and hemolytic in direct proportion to their surface tension lowering power. Surface active substances render the capillaries more permeable as demonstrated with T-1824 and account for the occurrence of pulmonary edema and death from shock after intravenous administration.

The droplet size is the limiting factor in emulsion stability both in vitro and in vivo. Electrolytes and globulins tend to break most emulsions while albumin tends to stabilize them. Different emulsions break at

varying rates when mixed with serum.

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Theoretical considerations and the above work show that, the preparation of fine emulsions by chemical means without emulsifying agents, and the use of water soluble dicarboxylic fatty acids compounds (or other synthetic fatty acids free of surface active properties), are worthy of future investigation.

#### FOOTNOTES

- \* Spans and Tweens were supplied through the couriesy of Atlas Powder Co., Wilmington, Del. Other materials were synthesized.
- \*\* Butyric Acid, furnished through the courtesy of Union Carbide & Chemical Corp.
- Furnished through the courtesy of E. Logeman Co., 377 Broadway, New York City.
  - Purified Bovine Plasma Fractions supplied through the courtesy of Armour & Co., Chicago, Ill.

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### **NUTRITION NOTES**

### EDUCATION IN NUTRITION

For many, if not the majority of practicing physicians, the subject of nutrition education is a particularly dry one. There is a superstition among doctors that too much violence of direction is likely to fall flat in this marter, and that inasmuch as innumerable generations of human beings have madaged to survive without any instructions about nutrition at appears superfluous now to start thinking about a subject which obviously entails ramifications of an endiese character. It is true that very little pressure has been excitanter, and once the subject is broached, the medical reaction is likely to be one of comparative indifference. Indeed, doctors may feel that such inspiration, arising as it must among the nutritionist, is essentially non-medical in its origin and consequently a suitable subject for their skeptical regard.

Logically, however, one is driven to the conclusion that shides of a very broad education in nutrition made available to school children possesses undeniable merits. Elizabeth A. Lockwood', of the department of Nutrition, Harvard School of Public Health, Boston, recently has promulgated this very conception, and she is probably correct in stating that if school children and school teachers could be given planned nutrition education as a part of their health programs, then within a comparatively short time there would be a nutrition-conscious public. It is true that the science of nutrition is

a rapidly changing one, but that is no reason why the unalterable fundamentals ought not to be taught. The subject really would need to be made a curricular one through all grades of school, and modified in conformity to the results of nutrition research.

We know that the generations of mankind which have appeared on the globe have always fallen far short of perfect nutrition, and the study of disease continues to indicate the increasing importance of nutrition in the prevention, cure and alleviation of illness. Perhaps the subject of nutrition is indeed not a completely inexhaustible store-house of undiscovered treasure, but there is little reason to doubt that, as we survey the entire medical field today, nutrition holds primary rank in its potentialities, so far as we are able to judge. Nutrition is not only the biggest thing in Medicine, it is also one of the biggest things in national welfare and in world-wide culture. It is appropriate that physicians, in particular, should lend their influence and support at community and state levels to the promulgation of sound nutrition education, which, in union with progressive research, holds much promise for the future solidarity, physically and mentally, of the human race. It is about time that educationists take up this problem seriously and, if necessary, displace less important subjects from the curricula to make room for nutrition and food study.

\*Lockwood, E. A.: Nutrition Education, Nutr. Rev., May, 1949, Vol. 7, No. 5, 129-131.

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### NUTRITION, A DYNAMIC INTERCHANGE

"The emergence of nutrition as a stream of material taking part in a dynamic interchange with the elements of the living protoplasm must surely revolutionize our approach to the subject of nutrition as the basis of normal health and function,'' recently stated Sir C. Stanton Hicks.\* It begins to appear, he continues, as if the living protoplasm of the cell is a protein enzyme structure, with vitamins as prosthetic groups, for the proper value from vitamin therapy appears attainable only if the diet is at the same time rich in protein. Amino acids after absorption from the gut are, for the most part, fashioned in the liver into aggregates which give the normal ninhydrin response of protein, and yet are small enough to traverse the capillary and cell boundary. They travel in the blood combined with the plasma protein which also is produced in the liver. The plasma proteins, the smaller protein aggregates just mentioned, and the remaining aminoacids form what has been termed the metabolic pool, be-tween which and the cell protoplasm a constant interchange of larger and smaller fragments and groups takes place under the influence of proteinases; the relative velocity of this interchange in either direction seems to be determined by the anterior lobe of the pituitary gland. Iron reaches newly formed red blood corpuscles in a matter of hours, thus indicating how rapid the interchange may be. Schoenheimer demonstrated the same dynamic equilibrium for depot fat. He showed that saturation and desaturation occurred in the liver and that depot fat could be mobilized and deposited there under the influence of what had been termed in the past, toxic agents. The function of fat metabolism in the liver is closely related to dietary intake of protein containing methionine, and hepatocellular damage will be hastened by a deficient intake of complete protein, and fat metabolism will be interfered with.

\*Hicks, C. S.: Physiological considerations in relation to hepatic disease. Med. J. Australia, April 23, 1949, Vol. 36, No. 17, 548-550.

### NUTRITIONAL DISEASE OF THE LIVER

A group of Australian physicians" has recently made an exhaustive study of what they call "nutritional disease of the liver." They feel that they correctly established the ctiology of the condition by comprehensive dietary histories, with additional data supplied by relatives and associates. Malnutrition was most frequently associated with alcoholism. The pathological condition of the liver showed a progression from fatty liver toward portal cirrhosis, and was followed by biopsies. The clinical diagnosis of hepatic disease was assisted by liver function tests. Thus, they feel that "chronic non-suppurative hepatitis" may be caused by prolonged malnutrition, or by the virus of infectious hepatitis, or by chronic biliary obstruction from stone or new growth. Additionally, prolonged exposure to chemicals in the form of drugs or industrial poisons may have the same effect.

The symptoms of this disease included lassitude, weakness, and mental impairment, anorexia, occasional hematemesis, but there was little or no jaundice. Associated vitamin deficiency manifestations often were present. Hepatic function tests

gave results which were within normal limits in early cases but became abnormal as portal cirrhosis was established.

Treatment consisted in removal of infection, correction of dietary errors, and the use of a high protein and high vitamin diet, with the inclusion of lipotropic substances such as choline. Under such a regime, early cases were cured and the downward trend of the severe advanced cases with portal cirrhosis may at least be retarded.

The authors emphasized that nutritional disease of the liver often remains undiagnosed, because it is not easy to obtain an accurate dietary history. In their 18 cases, 14 were associated with alcoholism. Other factors predisposing to malnutrition were occupational peculiarities, solitary existence, dietary fads and obsessions. Poverty was rarely encountered. Animal experiments by Himsworth in England and by Chaikoff in this country have shown that a low protein intake can produce hepatic necrosis and fibrosis. Gillman in Africa has shown similar changes in the human liver in protein deficiency.

Possibly the chief importance of this excellent contribution by Wood and his associates is to emphasize what appears to be a fact,—that we may find definite hepatic disease with enlarged livers resulting from protein starvation, and that, treated early enough by proteins of good biological value, cures may be obtained. Reading this paper also makes one wonder if alcoholic cirrhosis is not, after all, likely to be due to protein deprivation in the alcoholic, and not due directly to the effects of alcohol of the liver parenchyma.

\*Wood, J. J., Garlick, H. W., Motteram, R., Weiden, S., Moore, A., Mackay, M. and Turner, C. N.: Nutritional diseases of the liver. Med. J. Australia, April 23, 1949, Vol. 36, No. 17, 541-547.

### THE ANTI-THYROTOXIC EFFECTS OF VITAMIN B.,

Thus far (July 1949) no reports have appeared which might indicate any long-time failure of vitamin  ${\bf B}_{19}$  to maintain patients with pernicious anemia in satisfactory hematological and neurological remission, provided the substance is intra-muscularly administered in sufficient doses. It has already been noted that persons suffering from pernicious anemia, complicated by severe hypothyroidism, may require a higher dosage of thyroid extract than they needed prior to liver plicated by therapy. In some cases the dose has needed to be doubled to maintain a normal basal metabolic reading. That this phenomenon depends upon anti-thyrotoxic influence of vitamin B, itself now becomes clearer. Ershoff found that feeding liver combats thyrotoxicity in rats. It is now known that minute amounts of the new vitamin, in animal experiments, duplicate the growth properties of either fish solubles or injectable liver extracts, in animals which are receiving thyrotoxin. It is not impossible that vitamin B<sub>1,2</sub> may even tually find a sphere of usefulness in the treatment of thyroidism, although further investigation must precede use clinically for this purpose. In the interim, the practitioner should bear in mind that the administration of thyroid extract is less effective in patients who are being treated either with liver extract or vitamin B10.

\*Ershoff, B. H., Proc. Soc. Exp. Biol. Med., 64, 500 (1947).

### ABSTRACTS ON NUTRITION

Dauber, D. Herlick, L. and Katz, L. N.: The role of dessicated thyroid and polassium iodide in the cholesterolinduced atherosclerosis of the chicken. (Am. Heart J., July 1949, Vol. 38, No. 1, 25-33).

Dauber and Katz having previously discovered that the chicken was a more suitable experimental animal than the rabbit for studies in hardening of the arteries, the present authors, utilizing the chicken, fed dessicated thyroid and potassium iodide, together with cholesterol, in varying concentrations in an attempt to determine the effect, if any, of these substances on cholesterol induced atherosclerosis. While potassium iodide gave equivocal results, dessicated thyroid in doses of from 200 mg. per kilo per day to 1,000 mg. per kilo per day gave consistent results and gave protection against

arterial hardening proportional to the amount of thyroid used as compared with cholesterol. The thyroid minimized the rise in blood cholesterol levels seen in the cholesterol-fed control animals, and this inhibitor effect was maintained throughout the course of the experiment. In the potassium-iodide birds the blood levels of cholesterol were higher than in the controls.

Benson, R. A., Schneider, M., and Brand, D.: The use of rice as a cereal food in infants. (Arch. Pediat., May 1949, Vol. 66, No. 5, 209.

Rice is the least allergenic of all cereals and in a controlled feeding experiment of 47 normal infants, the use of Cream

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of Rice produced slightly better gain in weight than other cereals, and was well tolerated and accepted. The stools showed a somewhat increased amount of microscopic starch granules, but no particular significance should be attached to this finding. No gastro-intestinal disturbances occurred.

ABAD, M. B. AND PECACHE, L.: The pseudomeningitic form of infantile beriberi. (Acta Med. Philippina, Apr. June, 1949, Vol. V, No. 4, 21:27).

The authors present a useful description of a form of heriberiseen in the Philippines in breast-fed infants from 6 to 12 months old. Only 58 cases have been encountered by those pediatrists in 18 years. The clinical picture is that of a well-neurished or fairly neurished, breast-fed baby who has gradually become peaceful and quiet, as if he had forgotten how to cry, moan or smile. He wears a languid and indifferent look, his cyclids are but half open. Sometimes, in addition to the ptosis of the upper lids, there is strabismus or nystagmus, suggesting encephalitis or tuberculous meningitis. There is no nuchal rigidity. The therapeutic test in diagnosis is in-mediate, for the administration of 25 mgm. of thiamin chloride twice daily causes complete disappearance of symptoms in 2 or 3 days. The possible relationship of this syndrome to that of Wernicke is discussed.

Sorel, A. E., Besman, L. and Kramer, B.: Vitamin A absorption in the newborn. (Am. J. Dis. Child., May, 1949, Vol. 77, No. 5, 576-591).

Newborn children show diminished intestinal absorption of fats, especially vitamin A in oil, as compared with children above 1 year of age or adults. This was indicated by low vitamin absorption curves after giving oleum percomorphum in maize oil. Higher absorption curves resulted when the administered vitamin was dispersed in aqueous solution or when 16 per cent polyoxyethylene sorbitan monolaurate was used as the dispersing agent. This suggests the use of water as a dispersing agent in the giving of vitamin A to newborn children.

Schweigert, B. S.: The animal protein factor. (Nutrition Reviews, Aug. 1949, Vol. 7, No. 8, 225-227).

The term "animal protein factor" is used in a broad sense to include those growth factors which occur primarily in animal products, and includes chick growth factors obtained from cow manure, hen feces, fish solubles, liver extracts, and distiller's solubles; turkey growth factors, present in fish meal and fish solubles; hatchability and viability factors, obtained from cow manure, meat scraps, fish meal, and skim milk; the antipernicious anemia factor (vitamin B<sub>12</sub>) present in refined and crude liver extracts; growth and antianemia factors for dog, monkey, fox and mink, present in fresh liver, liver extracts and milk; rat growth factor (zoopherin) in crude casein, liver extract, fish solubles, hed and vitamin B<sub>12</sub> in distiller's solubles, rice polishings and liver extract; factor for reproduction and lactation, growth of rabbit, cotton rat and mouse, obtained from fresh liver, liver extracts, beef and 1:20 liver extract.

Vitamin  $B_{12}$  is of great value in the therapy of pernicious mnemia and possesses growth promoting properties for chicks, rats and for several microorganisms. Crystalline vitamin  $B_{12}$  elicits a response in pernicious anemia similar to that obtained with liver extracts, but whether the liver extracts contain factors needed in addition to vitamin  $B_{12}$  remains to be determined.

We now know of some 9 factors which are replaceable by folic acid (P. G. A.) or its variants. If we classify bacteria and fungi as plants then vitamin B<sub>12</sub> is not an exclusively animal factor inasmuch as it can be, and is, isolated from the cultures of streptomyces griseus, and is produced in fermentation liquors by many other microorganisms.

From the standpoint of over-all nutrition, the study of the "animal protein factor" has emphasized and rendered obvious, the desirability of including in the diet a wide variety of foods, including liberal quantities of foods from animal sources.

STRANSKY, E. AND ARAGON, G. T.: Anemia in pregnancy in the Philippines. Acta Med. Philippina. Jan. March 1949, Vol. V, No. 3, 25-39).

Blood studies of 204 pregnant women, almost at term, were undertaken and compared with a non-pregnant group. Blood values, even in health, are definitely lower in Filipinos than are found in other countries. Iron deficiency anemia is wide-spread among Filipinos, particularly in infants and pregnant women. This anemia is characterized by microcytosis and hypochromia. Macrocytic anemia of pregnancy seldom is seen in the Philippines, only one case in this series showing macrocytosis. This case was definitely hypochromic and seemed to be hemolytic in character. Iron deficiency anemia in pregnancy is one of the major medical problems in the Philippines.

ERNSTENE, A. C. AND PROUDFIT, W. L.: Differentiation of the changes in the Q-T interval in hypocalcemia and hypopotassemia. (Am. Heart J., Vol. 38, No. 2, 260-272).

The EKG findings are described in a typical case of hypocalecmia and in 5 cases of hypopotassemia due to various causes. Hypopotassemia is attended by rounded T waves of increased duration and usually low amplitude. When the widening of the T waves attains a sufficient degree, prolongation of the Q-T interval results. The RS-T segments are not lengthened but often are slightly depressed. Prominent U waves are commonly present and by partial fusion with the descending limb of the T waves may cause further apparent lengthening of the Q-T interval. The duration of the QRS complexes is occasionally increased.

In contrast to the findings in hypopotassemia, the EKG pattern in hypocalcemia is of a simple nature and consists entirely of prolongation of the Q-T interval due to lengthening of the RS-T segment.

Sappington, T. S. and Bockus, H. L.: Nitrogen metabolism in chronic idiopathic alcerative colitis and its therapeutic significance. (Ann. Int. Med., Vol. 31, No. 2, 929 200).

patients unquestionably suffering from idiopathic ulcerative colitis were carefully studied from the standpoint of protein metabolism by means of the familiar nitrogen balance determinations together with measurement of serum proteins, blood urea, red blood cell count and hematocrit. No patient was selected who had had any major surgical operation or major infectious illness within 3 months of the period of study. No studies were done during menstrua-tion, pregnancy, or in the presence of congestive cardiac The over-all nitrogen metabolism of the five patients was studied and all were found to have protein deficiency on admission to hospital. Positive nitrogen balance could be achieved and maintained in these patients by giving diets moderately high in protein with or without the parenteral administration of protein hydrolysate or blood. The hydrolysates appeared to be well utilized, but were probably not as beneficial as an equivalent amount of protein given orally. Large fecal losses of nitrogen were not common, and when present, seemed to be due to purulent or bloody exudate. No patient improved clinically unless positive nitrogen balance had been achieved and maintained. In four cases, positive nitrogen balance preceded clinical signs of improvement by several weeks. High protein feeding for several months may be necessary to correct the protein deficit in these patients. The authors make no claim that chronic ulcerative colitis is primarily a manifestation of protein deficiency. Chemotherapy, psychotherapy and antibiotics are all necessary in treatment, but, nevertheless, a positive mitrogen balance appears to be one of the necessary conditions for clinical

### **EDITORIAL**

### HEARTBURN AND SIMILAR GASTRIC COMPLAINTS

The many manifestations of the common symptom called heartburn undoubtedly led Dr. Alvarez (1) to make the statement "That only after practicing medicine more than 30 years did it occur to him just what heartburn was." A number of terms are applied to the condition namely, (2) Heartburn, Pyrosis, Flatulence, Eructations of gas, and Belching. We find these and similar terms associated with regurgitation, sour and bitter, burning, acid, epigastric and abdominal pain, as well as nausea and vomiting, nervous tension and fatigue. Heartburn is probably not due to any organic change within the gastro-intestinal tract, Tumen and Cohn (3). It is not due to an excessive gastric acidity, Rehfuss (4), who also states that it is not a symptom of ulcer. M. Einhorn (3) also doubts that it is due to the influence of acid gastric juice. Alvarez also noted that of 17 patients with ulcers, heartburn bothered them only when the ulcer seemed to be healed and not while the ulcer was active.

Flatulence is one of the most common of all gastric complaints Rehfuss (4). It has been noted in the presence of achlorhydria by Babey (6), and Barsonay and Szemso (7) who also found that by instillations of Dilute Hydrochloric Acid, heartburn would disappear while the installation of alkalies increased the heartburn.

Psychogenie factors associated with abnormal neuro-muscular activity above the cardia may produce reverse peristaltic waves and be factors in producing heartburn, (Tumen-Colnu) however, Refuss states that a "Diagnosis of anxiety states, frustrations, etc., only cause the patient to shop around from Doctor to Doctor." He also stresses the importance of skill in "Cross-examination" of the patient, in order to clicit the real facts, putting them in a correct perspective, which is essential to a correct diagnosis.

Best & Taylor (5), describe human digestive juice after a test meal as having a normal acidity of 0.05 to 0.15% and usually not above 0.1%. At the height of digestion of a mixed meal the % is around 0.3%, the pH of 1.3 to 2.50: Alkalies have a depressing effect on the secretion of gastric juice. Regurgitation of alkaline duodenal contents into the stomach may be a factor in reducing the acidity of the stomach.

The production of stomach and intestinal gases by interference with the circulation of the bowel or by reflex reaction, Alvarez (16), or by any condition that favors reverse peristalsis, is especially true in the case of users of laxatives and eatharties which propel the intestinal contents, before they are properly prepared by digestion for that onward movement.

The frequency of heartburn during pregnancy gives distinction to the ailment. It has been established that the gustric acidity decreases as the pregnancy advances, Chemical analysis of the gastric juice shook the foundation of alkaline therapy when it was found that conditions of hypoacidity and often anneidity of the gastric juice were generally present. Consequently Hydrochloric Acid has been tried effectively in many cases, Williams (8). More than 30 years ago while in general practice I also found that Dilute Hydrochloric Acid often relieved the fletylewes of pregnancy.

practice I may found the relieved the flatulence of pregnancy.

Dr. Chas. H. Nielson (9) showed by a large number of experiments on medical students and others that taking water alone even stimulated the secretion of digestive juices. This was further confirmed by Hawk (10) and by Rehfuss (11). The writer found that taking water with meals objaices the necessity for various remedies taken for constipation (12). Nielson further taught that "Fermentation in the stomach

was often due to organic acids, while the prevence of mineral acids prevented fermentation."

Ulcer, either gastric or duodenal, biliary disease or disease of neighboring structures are excluded from this discussion of heartburn, flatulence, eructing gas or any other name applied to the same complaint.

For years in a large general medical clinic, where I have seen a very large number of patients, the symptom "Eructs Gas" has been noted and found to be one of the most common complaints. Upon close cross-questioning of the patient the fact was clicited that a great majority of these patients were taking laxatives or catharties and also taking "Soda" or other forms of antacids. They also did not "Take any water with their meals." Many of those post-ulcer cases that had undergone medical or surgical treatment, or both, and apparently were healed, but were having gastric complaints, were made more comfortable by giving them Dilute Hydro-chloric Acid.

The nervous element present in most of these cases was relieved by giving Phenobarbitol gr 1/4 before meals. The Dilute Hydrochloric acid to restore the normal gastrie acidity, was given in water and with their meals, instead of in orange juice, since it was shown by Sansom (14 & 15) that the latter contributes to the alkaline side of digestion.

#### CONCLUSIONS

1. Heartburn and similar terms refer to a "Functional" Stomach disturbance. 2. Discontinue the use of Laxatives, Catharties and Ant-Acid remedies. 3. Restore normal Gastric Acidity. 4. Take an adequate amount of water with meals, to secure a normal or physiologic digestion.

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### **BOOK REVIEW**

Physiology in Diseases of the Heart and Lungs. M. D. Altschule, M.D., 368 pages. Harvard University Press, Cambridge, Mass., 1949, \$5.00.

This valuable text may be said to explain why the cardiac or pulmonary case presents the signs and symptoms he does present. It is a complete, systematic and critical review of available studies in human disease of the heart and lungs. Once the processes underlying symptoms are clarified, the mechanisms by which therapy is effective, become obvious. A unique feature of book is a large bibliography, quite exhaustive in nature. It should prove of special value to investigators, teachers and specialists in the field of heart and lung disease.

### GENERAL ABSTRACTS OF CURRENT LITERATURE

Castleton, Kenneth B. and Dolowitz David A. Peptic ulcer of the esophagus with severe bleeding controlled by aryccl. Gastroenterology 10, 5,797. May, 1948.

Peptic ulcer of the lower end of the esophagus probably occurs more commonly than has been generally suspected. A case is reported of bleeding esophageal ulcer in which the artery was observed through the esophagoscope. The hemorrhage was so severe that preoperative transfusions of 2500 cem of blood did not prevent the patient from being virtually exsanguinated. Oxycel applied topically was successful in controlling the hemorrhage. Subtotal gastric resection had been performed in the mistaken belief that bleeding was gastric or duodenal in origin. It is suggested that in cases where diagnosis is uncertain preoperative esophagoscopy may be of value. It is suggested that local application of oxycel may be used to control bleeding from esophageal varices as well as from ulcers.

Franz J. Lust

Nissen, Rudolff. Bridging of esophageal defect by pedanculated flap of lung tissue. Annals of Surg. 129, 1,142, January, 1949.

A 56 year old male patient was admitted with a brief history of esophageal obstruction. Roentgenographs revealed a half-moon shaped filling defect of the middle portion of the thoracic esophagus. The roentgenologic diagnosis was benign tumor, probably leiomyoma. The esophagoscopy and biopsy revealed small ulcerations of the mucosa in the obstructed area. The impression of the endoscopist was also that of a submucous benign tumor.

At operation, the left thoracic cavity was entered through the bed of the 6th rib. A large tumor of the muscular sheath of the esophagus was found, extending from the inferior margin of the acrtic arch to two inches below the level of the bifurcation. The tumor mass occupied the entire circumference of the esophagus. In order to expose and excise it, two segmental arteries arising from the descending acrta had to be severed. The muscle tube comprising the entire muscular wall of the esophagus was partly interwoven with and greatly thinned out by the tumor. In order to insure radical removal, the entire muscular tube was removed with the neoplasm. After completion of the excision there remained a muscular cylinder 10 cm in length, deprived of muscular sheath.

Since the vascular supply of this demided area was probably insufficient because of the ligation of two segmental arteries and the sear formation in the mucosa, it was felt that the denuded area should be covered by viable tissue. Therefore, the adjacent upper segment of the lower lobe of the lung was mobilized and wrapped around this portion of the esophagus. A complete cover was thus obtained. The lung was fastened to the muscular sheath of the esophagus above and below the defect, in a manner demonstrated on excellent drawings, accompanying the article. The phrenic nerve was crushed above the diaphragm a rubber catheter inserted through a separate stab wound in the 9th intercostal space and the incision of the chest wall closed in layers. The microscopic examination of the specimen confirmed the diagnosis of a leiomyoma.

Franz J. Lust.

Temple, L. J.: Treatment of perforations of the oesophagus. (Brit. Med. J., May 28, 1949, 935-937).

Tearing by foreign bodies, including esophagoscopes, is the commonest cause of esophageal perforation. The surgeon who believes he has perforated the esophagos during an endoscopy should, if facilities are available, have the anesthesia continued, turn the patient over and open the thorax and at once proceed to do a gastrostony. Early drainage of the mediastinum into the pleura is essential. Early diagnosis and primary suture of the instrumental or foreign body tear of the thoracie esophagus is siressed. Conservative treatment for suspected damage to the cervical esophagus is sometimes successful, but the surgeon must be ready to interfere at once should cellulitis appear.

Melamed, M. and Melamed, A.: Prolapsed gastric mucosa: a possible cause of "gastric" symptoms in right heart failure. (An. Int. Med., August 1949, Vol. 31, No. 2, 245-259).

The diagnosis of prolapsed gastric mucosa can only be established, during life, by X-ray examination and the condition, which may be more common than generally considered, onght to be looked for in "atypical peptic ulcer" symptoms. The finding of gastric mucosa prolapsed into the duodenum at post-mortem, in patients dying of congestive heart failure, is an argument supporting the authors' thesis that such cardiac disease may be a common cause of the mucosal prolapse, through the production of gastric congestion. Four cases are presented in which gastric symptoms were presented and in which autopsy showed herniation of stomach mucosa into the duodenum. In two of these cases, X-ray studies of the duodenum during life was diagnostic of mucosal prolapse.

One patient suffered from arteriosclerotic heart disease and another from right heart failure secondary to chronic asthma and pulmonary fibrosis. The prolapse of gastric mucosa can be reversible and disappear with subsidence of edema and congestion of the stomach during periods of cardiac improvement. It is felt that right heart failure, in particular, ought to be regarded as a possible cause of prolapse of gastric mucosa into the duodenum.

HILLEMAND P., MARKE P., CARRAYON, MRS.: Primary gastric localisation of Lymphogranulomatosis malignans. Les localisations gastriques primitives de la lymphogranulomatoes maligne. Archives des maladies de la Digestion et des maladies de la nutrition, Volume 38. No. 1 and 2, January-February, 1949.

According to these authors gastric localisation of Lymphogranulomatosis malignans can be classified in two categories: lst: Gastric localisation appearing in the course of Hodgkin disease; 2d: Primary gastric localisation of the disease. This second category derives its importance from the fact that it is surgically curable due to its very slow evolution which keeps it localised through a long period of time.—The authors have observed three cases of this disease; forty are known in the literature, six of which were published by French scientists.

The etiology reveals that it is a rare disease which generally affects middle age people. The symptomatology consists of: Functional symptoms: Localised epigastric pains irradiating towards the back, comiting, pyrosis, anorexia, hemorrhage; General symptoms: asthenia, loss of weight, and, contrary to Hodgkin in general, no persisting fever; Physical symptoms: loss of weight, pallor; Hemogramm: RBC: 3.000.000; WBC: 10.000, Eosinophiles: 2,3 and up to five. Gastric chemistry shows: Total acidity 19.52, free HCL reduced, Hypochlorhydria, rarely Achlorhydria.—The gastroscopy reveals: a) Ulcerations with profuse mucus secretion localised on the posterior walls (in two cases only published by Koenig): in the upper two thirds of the stomach, according to Browne and McHardy; b) Hyperplasia of the polype type, this hyperplasia is not rigid.—Clinical aspects: the disease appears like: a) an ulcus; b) a CA of the stomach with evolution of varied duration and presenting many forms: An ulcerative type, an infiltrating type, a type simulating a pyloric stenosis, a type simulating an ulcerated pyloric stenosis, a cancerous evolution of an ulcus (Titu Vasiliu and Singer), a hemorrhagic type (Laus), an anemic from (Guttman), transit disturbances, usually a slowing down and showing no wall signs, a pseudosyphilitic form with no other precise sign but a positive Wasserman, all of which permits following deduction:

The clinical types of primary Lymphogranulomatosis malignans are very varied, which makes a diagnosis impossible. A few indices only allow a presumption: a) the slow evolution; b) the contrast between a large tumor of the stomach and pretty good general health maintenance; c) no worsening of the X-ray picture after several months of evolution; d) some X-ray and gastroscopic signs like the contrast between the expansion of the lesion and its relative extensibility. Diagnosis.—Can be ascertained by pathological and histological examination only. One typical aspect.—Localisation, in the antrum

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generally, partially or totally invaded, preferably small curvature and posterior wall; in two cases invasion of the cardia, in two cases invasion of the oesophagus, in some cases invasion of pylorus and bulbus duodeni .- Size: From walnut size to large orange, subscrous; the tumor invades rapidly the lumen of the stomach thus causing transit disturbances .the surface is covered with roundish irregularities and hypertrophied folds. The color is greyish white. Of greatest portance is the following: the consistency is soft, elastic (sign for the surgeon who thought to operate a Ca); no induration. no adhesion to surrounding organs but perigastric adenopathy. The histological examination reveals polymorph cell proliferation with diverse polynuclear; large amount of cosinophiles, some monocytes and plasmocytes invading deeply into the muscularis mucosae, and large amount of large Sternberg cells, characteristic for Lymphogranulomatosis malignans. Pathogenia: Probably from mesenehymal elements of the gastric wall. The treatment suggested is a) Surgical: Gastrectomy or gastroenterostomy; the mortality is 50% in the first week; some cases survive 6.8 years after operation, some cases relapse, b) X-ray therapy: Some authors advocate early energetic irradiation strictly localised; some prefer late irradiation in case of relapse.

Jules Pierre, M.D.

Walters, W., Berkson, J.: Carcinoma and other maliquant lesions of the stomach. (Miss. Valley M. J., July 1949, Vol. 71, No. 4, 129-130).

The only hope for cure of gastric cancer lies in operation following early diagnosis. A routine yearly examination of normal persons, including X-ray studies of the stomach, is suggested. The operation rate and resectability rate of cancer of the stomach has gradually increased at the Mayo Clinic, and the survival rate for 5 years or longer is 28.6 percent. Survival rate is higher in those with higher amounts of gastric acid and in those with low-grade lesions. Younger persons have less likelihood of surviving 5 years after operation than do older persons. The use of radiation therapy is useful in lymphosarcoma of the stomach but no value in adeno-carcinoma, fibrosarcoma or leiomyosarcoma.

HANDLEY, R. S: Chronic ileus caused by malignant invasion of the posterior abdominal wall. (Brit. Med. J., May 21, 1949).

Sir Heneage Ogilvie (1948) describes two cases in which invasion of the crura of the diaphragm, celiac axis, and semilunar ganglia by malignant tumor produced functional paralysis of the bowel which mimicked obstruction. The author adds a fourth case (Dunlop reporting a third case in the same issue of the same journal) in which invasion of the same area resulted from what was probably a cancer of the panereas, producing symptoms suggestive of small bowel obstruction. Constipation, vomiting and right lower quadrant tenderness suggested adhesions between the terminal ileum and an old right paramedian appendectomy scar. Roentgen examination suggested partial obstruction in the ileum. At operation, the ileum was found moderately distended, but no obstruction was found. The pancreas contained a growth spanning the aorta, fixed to the posterior abdominal wall, and Following operation progressive distention occurred and he died on the fourth day, no autopsy being obtained. Ogilvie, who was the first to describe such a case, felt that sympathetic paresis from tumor invasion was the cause although in the absence of a post-mortem examination in this case, his theory could not be completely substantiated.

DUNLOP, J. A.: Ogilvie's syndrome of false colonic ob struction, (Brit. Med. J., May 21, 1949, 890-891).

A syndrome of large bowel obstruction thought to be due to sympathetic deprivation was recently described by Heneage Ogilvic (1948) with a report of two cases, including findings, but without the possibility of full conlaparotomy firmation of the suggested anatomical diagnosis by postmortem examination. The author presents another case with full autopsy findings. The presenting symptoms were those of colonic obstruction, although no lesion could be demonstrated in the colon by clinical or roentgenological examination. The primary lexion was an extensive cancer of the left lower The bronchus with secondaries in many organs, including the glands

of the pre-aortic region. The efferent nerves from the left side of the semilunar ganglion passed directly into a car-cinomatous mass. Such a syndrome can occur only where efferent sympathetics are affected and efferents spared. In this case the dysfunction involved the lower ileum and proximal colon and this will probably be found to be a general rule in such cases. The lesion affects the mid-gut rather than the hind-gut.

D'Albora, JCHN B. AND INGEGNO, ALFRED P. Carcinoid tumors of the small bowel. Gastroenterology 10, 2, 310. February, 1948.

Four instances of operatively demonstrated small intestinal carcinoid are reported. All were in the ileum, Two had caused infestinal obstruction. One had produced metastatic tumefaction of mesenteric nodes discovered on routine examination. The fourth case was an unusual combination of symptomatic Meckel's diverticulum and carcinoid, the latter being an incidental finding. The difficulties of diagnosis are emphasized by the fact that the nature of the lesion was not suspected pre-operatively in spite of careful study. Carcinoids of the small bowel are unusual but constitute a relatively high production of symptomatic small intestinal tumors. A resume of their origin, character, and symptomatology is given. presence should be particularly suspected in middle-aged or elderly individuals with a long standing history of digestive disturbance and episodes suggesting partial intestinal ob-struction. Surgical resection, even in the presence of meta-statis, is the treatment of choice and the prognosis is rela-tively good. Three of the patients are alive 10, 16 and 75 months after operation.

Franz J. Lust.

LORBEER, STANLEY H. AND MACHELLA, THOMAS E.: Enteric cust of the duodenum, Gastroenterology, 10, 5, 892, May, 1948

An enteric cyst of the duodenum is reported and the literature on such tumors is reviewed,

The roentgenological examination after barium meal revealed a probable tumor of the second portion of the duodenum To establish the diagnosis a technic used by the authors and described by Shiffer was employed. The third portion of the duodenum was intubated with a double lumened Miller-Abbott tube, one lumen of which communicated with a distally placed balloon capable of holding 50 cem of air. Inflation of the balloon in the lower duodenum produced pain similar to that about which the patient had previously complained. A barium suspension was injected through the other lumen of the tube jeto the section of the duodenum proximal to the balloon The tumor was clearly delineated in the second portion of the duodenum by this method,

Franz J. Lust.

WILTRAKIS, G. A. AND HUDELL, J. C.: Regional ileitis and neurosis. (Illinois Med. J., June 1949, Vol. 95, No. 6, 360-363).

A case is presented, which under good medical auspices. was diagnosed psychoneurosis, but laparotomy revealed stenosing regional ileitis. This brings up the old question as to whether or not psychogenic factors contribute to the cause of this disease.

MEYER A. C. AND MATHEWS, A. R. K.: Acute regional ileitis in an 80-year-old male. (Ill. Med. J., June, 1949, Vol. 95, No. 6, 367-368).

This is the oldest patient to have been reported suffering from neute regional ileitis. Following a short-circuiting operation there was a marked resolution of the lesions over a three week period.

NELSON, T. Y .: The place of hydrostatic pressure in the treatment of intusxusception. (Med. J. Australia, June 25, 1949, 825-827).

An analysis of the treatment of 102 patients (of the author's) with intussusception is given, hydrostatic pressure being used as a preliminary to operation. In 20 cases the intussusception was reduced without operation and in a further 23 cases it was found reduced at operation. The death rate

of the series was 9.8 percent. The method is of definite value. Conservative methods ought to be used in all cases examined in the first twenty-four hours. The author regards the method of reduction by a barium enema under fluorescopic control as deserving further investigation.

TAYLOR, J., POWELL, B. W. AND WRIGHT, J.: Infantile diarrhea and vomiting, (Brit. Med. J., July 16, 1949, 117-125).

This paper reports a clinical and bacteriological investigation of infantile diarrhea and vomiting usually occurring in outbreaks of the disease. No recognized intestinal pathogen was isolated and virus investigations in fatal cases yielded negative results. Bact. Coli sera prepared from strains isolated from certain cases led to the identification of a particular serological type referred to as Bact. Coli D433. It was isolated from all nine cases examined during life in one of the outbreaks investigated and in an extremely high percentage (91%-100%) in certain other outbreaks, but it was less frequent in still others and absent in one group. This organism was not isolated from any of the 208 control babies. Further research is needed to determine whether the serological type of Bact. Coli has any etiological significance in this disease.

MALMROS, H., WILANDER, O. AND HERNER, B.: Inoculation hepatitis. (Brit. Med. J., Nov. 27, 1948, 936-938).

The authors have shown that hepatitis usually referred to as "homologous serum jaundice" similar to common epidemic infective hepatitis), may be produced accidentally by the drawing of venous or capillary blood or by serum, plasma or blood transfusions or intravenous or intramuscular injections where a sterile instrument is not used. The so-called blood-gun used in making blood counts is extremely risky to use, being difficult to sterilize and should be replaced by a needle-holder and exchangeable gramophone needles.

Morton, R. S.: Syringe-transmitted jaundice. (Brit. Med. J., Nov. 27, 1948, 938-939).

An investigation was made into the continued incidence of jaundice in a V. D. clinic where sterilization was thought to be adequate but it was found that on busy days, insufficient caution had been observed in sterile technique. All syringes must be individually sterilized for each injection or blood sampling in order to control syringe-transmitted jaundice.

Silva, G. S. P. S.: A simple method of computing the volume of the gallbladder. (Radiol., Jan. 1949, Vol. 52, No. 1, 94-101).

The writer has described, in this article, a simple method of computing the volume of the gallbladder. A tracing of the cholecystogram, made on transparent paper, is placed apon a ruled paper with parallel and equidistant lines, thus dividing it into a series of segments or "disks." The diameters of these segments are measured in millimeters with he aid of a ruler, and the volumes corresponding to the diameters of these segments are found in an accompanying table. The sum of these individual volumes is multiplied by a correction factor (to compensate for magnification of the image shown in the film), and the result is the volume of the gallbladder in cubic centimeters.

CHAMSI, CH. BERDJIS: Roussy's Cirrhosis of the Liver (Senile Cirrhosis) Its Connection With Endocrine Glands and Especially the Parathyroids. Archives Des Maladies de L'appareil Digestif et Des Maladies de la Nutrition 38,3, 153, March, April, 1949.

In 50 cases of obstructive cirrhosis of a special type examined at the Cancer Institute in Paris and at the Pathological Institute in Geneva, the authors made the following characteristic observations:

Anatomically, the liver shows definite changes, such as, that the consistency is increased, the parenchyma is barder,

more resistant and dryer than normal. The surface of the liver has a smooth appearance, with fine, regular granulations. The color is darker. Histologically, the examination revealed the presence of the general characteristics of cirrhosis, but less distinct, and more outspoken. The interstitium is scierotic. The spaces of Kiernan are disconnected, there is a tendency of pseudo-lobular formations. There is an infiltration of lymphocytes and there are some signs of regeneration of liver cells. Clinically, there is an absence of definite signs of portal retention, such as ascites and collateral blood circulation. In all cases some signs of liver insufficiency can be found. The endocrine glands are atrophied in the course of ordinary cirrhosis, however, very little changes in Senile Cirrhosis. The parathyroids are changed differently in these two groups of cirrhosis:

A. There is a definite hyperfunction in ordinary cirrhosis.

B. There are only rich oxyphile cells in Roussy's cirrhosis.

Roussy's cirrhosis is therefore, a special disease, with definite clinical and pathological and anatomical changes, especially of the parathyroids.

Franz J. Lust.

Walters, W.: Treatment of biliary obstruction (Texas State J. Med., Jan. 1949, Vol. 45, No. 1, 18-24)

The author makes the important point that although the gall bladder may be regarded negative or normal from an X-ray standpoint, this does not always exclude the possibility that stones which are non-opaque to roentgen rays may be situated in the interior. Patients with a history of repeated biliary colies should be suspected of having disease of the biliary tract even when a cholecystogram fails to give evidence of it. Angina pectoris is not infrequently wrongly diagnosed, hecause precordial pain has been produced experimentally by an increase in the pressure within the ducts of the biliary system. Stricture of the common and hepatic bile ducts usually results from injury occasioned in the course of operations on the extra-hepatic ducts. Persistent jaundice results. Successful surgical repair of such stricture now is the rule. Biliary dyskinesia due to spasm of the sphineter of Oddi is corrected by an anastomosis between the common duct and the duodenum, and this usually relieves colic due to this cause. Cancer of the bile ducts is rare. When the carcinoma is in the head of the panereas, resection of the head along with the ampulla of Vater with the attached portion of the duodenum is proving increasingly valuable as a life-prolonging operation.

Russell, Walter A., Weintraub, Sydney, and Temple. Harold L.: An analysis of X-ray findings in 405 cases of benign gastric and pyloris ulcers. Radiology 51,6,790. Dec., 1948.

The confusion in anatomical terminology in reference to the stomach is emphasized, and a plea is made for the adortion of precise nomenclature to be used and understood equally well by the roentgenologist, surgeon, and pathologist.

Of 429 ulcers in 405 cases, 65% occurred on the lesser curvature of the body of the stomach, including the region of the incisura angularis. A relatively high number, 8%, were located in the preplyoric area, 19 occurred at the pylorus. The radiographic criteria for diagnosis of pyloric ulcers are given. The reason for the discrepancies between the radiographic and surgical location of a lesion, particularly in the region of the pylorus, is discussed. It is the opinion of the author that the X-ray diagnosis of location is by far the more accurate. A comparison is made between the results of the medical and surgical treatment in patients requiring hospitalization. The treatment of choice is gastric resection, which showed 92% good results as compared with 41% for medical management. Multiple gastric ulcers were observed in 23 cases (5.7%). Triple ulcers were seen once. In the case of triple ulcers and in 10 instances of double ulcers, the lesions were observed simultantonsly. Duodenal ulcers, either active or healed, were associated with gastric ulcers in 10%. Franz J. Lust.

The American Board of Internal Medicine announces oral examinations in the subspecialty of Gastroenterology as follows:

February 10, 11, 1950 at Chicago, Illinois.

April 14, 15, 1950 at Boston, Mass.

June 23, 24, 1950 at San Francisco, California.

These examinations are for candidates who have been certified in Internal Medicine and who have made application and passed the Gastroenterology.

Albert F. R. Andresen, Chairman Subspecialty Board in Gastroenterology.

### SCHERING DISCOVERS NEW MOST POTENT ANTIHISTA-MINE DRUG

A new, most potent of all safe antihistaminics now known, Chlor-Trimeton maleate, has been developed by the chemical and clinical research groups of Schering Corporation, pharmaceutical manufacturers of Bloomfield, New Jersey. The drug, which has just been released for the use of the medical profession, is about twenty times as potent as the other currently available drugs with similar activities.

The antihistaminic drugs are generally used in the treatment of hav fever, asthma and other allergies. Drugs of this general class are believed to block the action of histamine. The action of Chlor-Trimeton in this respect is specific and so potent as to make it many times as effective on a weight basis as the previously available antihistaminic drugs. Because of its high activity, Chlor-Trimeton can be used in minute doses (only 2 to 4 milligrams). Because of the minute quantity taken, its action is usually free of the undesirable side effects (sleepiness nausea, dizziness) so common with the previous drugs.

The parent drug of this substance is prophenpyridamine (Trimeton). The latter differs in fundamental chemical structure from the other antihistamine drugs known to have similar actions in the body. Chlor-Trimeton, as its name indicates, is derived from prophenpyridamine by substituting a single chlorine atom for one of its hydrogen atoms and the formation of

maleate salt. Chlorination of prophenpyridamine has yielded a much more potent substance, while it is interesting to note that chlorination of the other most widely-used antihistaminies has not increased their potency. The new Schering drug is claimed to be not only the most potent anti-histamine and with minimal side actions, but also that with the lowest dosage.

On the basis of animal studies Chlor-Trimeton was shown to have several very desirable properties: Its antihistamine effect was very quick and direct, and its activity was manifest in very small doses; and the animals, even on large doses, show no undesirable effects.

It is already well established that the compound is effective in a very small dose, in a range which was unheard of before the appearance of this drug. Secondly, the side effects, a common shortcoming of most of the presently available related drugs, have been reduced to a bare minimum, about 5 percent of those under treatment reporting slight undesirable side actions.

#### PRURITUS

MY-B-DEN (Adenosine-5-Monophosphate, Bischoff) now available for Systemic Therapy of pruritus.

A new approach to effective treatment of pruritus is announced by Ernst Bischoff Company, Inc., Ivoryton, Connecticut, with the release of MY-B-DEN. In the majority of cases studied thus far, this unique compound has produced complete subsidence or marked amelioration of symptoms. Beneficial results have been reported in generalized pruritus, pruritus ani, pruritus vulvae, pruritus scroti and in cases of Hodgkin's disease, dermatitis herpetiformis, diabetes mellitus, obstructive jaundice and hair dve sensitivity.

MY-B-DEN is thought to correct the altered phosphorylation mechanism responsible for pruritus and certain forms of skin disease. This unique biochemical is intimately related to basic life processes and is a vital metabolic link in muscular contraction and enzymic reactions. Clinical and pharmacologic studies indicate an important role for MY-B-DEN in the treatment of vascular disturbances, cardiovascular disorders and degenerative diseases.

MY-B-DEN is supplied in 1 cc. ampules in boxes of six. Each capsule contains 20 mg. per cc. of the crystalline-free acid as a sodium salt.

Drug list retail price, \$9.83 for a box of six ampules 1 cc.

# ASSOCIATE SALES MANAGER NAMED BY BREON

Appointment of Charles L. Czermak as associate sales manager of George A. Breon & Company, manufacturing pharmaceutical chemists, was announced recently by J. Gill Jordan, president. Mr. Czermak, who joined the Breon sales force in 1946, will assist in the planning of sales and merchandising activities and in the supervision of the sales personnel.

Born in Brooklyn, N. Y. on December 13, 1913, Mr. Czermak received the B. S. degree from the University of Alabama, majoring in sciences and physical education and participating in varsity athletics for three years. After getting a tryout with the New York Yankees, he taught and coached athletics at the Carrollton High School, Carrollton, Ala., from 1936 to 1941, and served in the U. S. Navy during the war.

Mr. Czermak is married to the former Marjorie Wimberley of Reform, Ala., whose father, Dr. G. B. Wimberley, has been in general medical practice in that locality for 55 years. Mr. Czermak is a member of Phi Sigma fraternity, the American Legion and the Veterans of Foreign Wars.

## MILLION DOLLAR LIBEL SUITS

Two one million dollar libel suits were announced in 1949 by Dr. Anton J. Carlson, President of the National Society for Medical Research. "To appreciate the real significance of this legal action," Dr. Carlson stated, "one has to be aware of the facts behind the most overt villification-orgy of our times." Dr. Carlson pointed out that no campaign of our century has continually carried as much irresponsible lying, maliciousness, and defamation as the one aimed at the doctor and the medical science researcher as the so-called "vivisector."

"That the same people," Dr.

# now

# peptomatic digestional aid in single tablet form

By developing an entirely new type of enzymatic carrier, literally "a tablet within a tablet," Robins now makes available a triple-enzyme digestant—Entozyme. In one small specially constructed tablet, Entozyme "packs" pepsin, pancreatin and bile salts—in such a way that they are released only at the gastro-intestinal level of optimal activity. Thus Entozyme greatly simplifies and makes more effective the treatment of complex digestive disturbances of the gastro-intestinal tract. Clinical studies 1.2.3 have demonstrated the value of Entozyme in such conditions as chronic cholecystitis, chronic duodenal ulcer, acute and chronic pancreatitis and certain postoperative syndromes of the gastro-intestinal tract—in relieving nausea, belching, distention, anorexia, food tolerance, etc.

FORMULA: Each specially constructed tablet contains Pancreatin, U.S.P., 300 mg.; Pepsin, N.F., 250 mg.; Bile Salts, 150 mg.

**DOSAGE:** One or two tablets after each meal, or as directed by physician, without crushing or chewing.

AVAILABLE: Bottles of 25 and 100.

### REFERENCES:

- 1. Kammandel, N. et al.: Awaiting publication.
- McGavack, T. H. and Klotz, S. D.: Bull. Flower Fifth Ave. Hosp., 9:61, 1946.
- Weissberg, J., McGavack, T. H. and Boyd, Linn J.: Am. J. Digest. Dis., 15:332, 1948.

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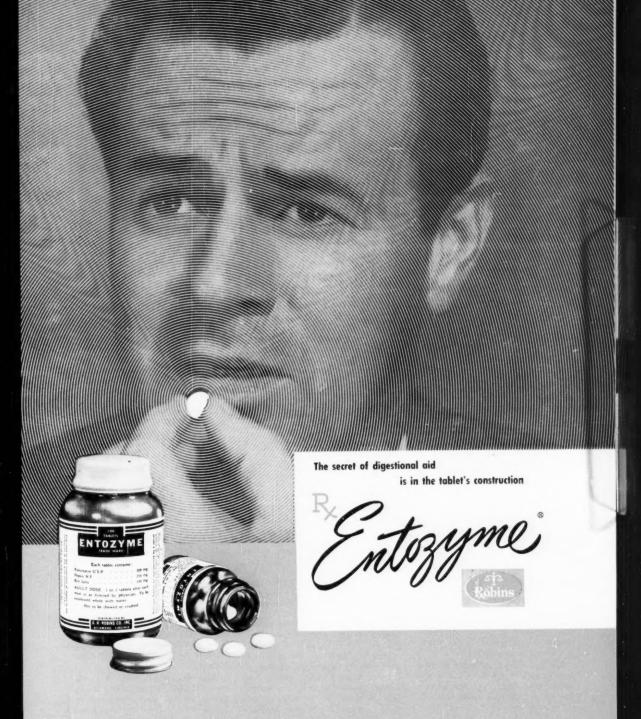


Releases pepsin in the stomach



Releases pancreatin and bile salts

\*The "Peptomatic" Tablet —
a coined word to describe the unique
mechanical action of Entozyme Tablet.



Carlson continued, "to whom we turn to in our most trying moments and who have given us such health-protecting and pain-alleviating wonders as insulin, anesthesia, blood transfusion, surgery, penicillin, and many other safeguards of life for man and animal alike, and on whom we depend for the conquest of such scourges as cancer, polio and heart disease should be branded day after day and year after years as 'sadists, mutilators, tormentors, and vicious cruel torture-mongers' is beyond belief.

Probably this happens, Dr. Carlson said, because the medical scientist generally stands alone. . . The stereotype of the scientist as a quiet man, leery of noise and crowds, and unaware of the sociallegal entanglements of his time. If he is to produce for us, he must necessarily be absorbed in his laboratory. "When the small irresponsible group of antivivisectionists and their public mouthpiece, the Hearst Press, picked out the medical scientist as their 'defamation goat', they picked out a person who didn't have the time, the temperament, or the weapons to fight back.

"But," Dr. Carlson added, "events of recent years, ranging from actual violence, slowing of research, and stoppage of medical training to general and personal villification on its lowest level have forced the doctors and scientists to take time, to adjust their temperaments, and to utilize the democratic weapons, of organization and law to fight back. Now the fight on the legal front is just beginning, and this issue is joined.

"Two million dollar libel suits have been filed by medical scientists against the Hearst Publishing Company and William Randolph Hearst. Two more are pending, and other suits will follow if necessary. This is the beginning of a policy which took shape when a nationwide legal committee was formed by the National Society for Medical Research to advance medical research and to protect the medical worker and his institution against what appears to be an organized program to villify and slander medical science and scientists.

Medical science asks for no immunity against criticism, but it refuses to be 'the goat' any longer for the ugliest and most baseless villification campaign of our times. A counter attack in the courts against this calumny will be pursued to the utmost. With slanderous falsehoods prohibited by law, Dr. Carlson concluded, "there will be practically nothing for the antivivisectionists and their 'reporters' to report."

One million dollars for punitive and compensatory damages is being asked by Dr. N. R. Brewer of the University of Chicago in his libel suit just filed in the United States District Court against the Hearst Publishing Company, Inc., publisher of the Chicago "Herald-American", and William Randolph Hearst of San Simeon, California.

Pictures of Dr. Brewer holding dogs which were described in the captions as "tortured" and "tormented", and references to Dr. Brewer in news articles and editorials as "torturer", a "sadist", and a "cruel experimenter" were referred to in the complaint by the doctor who is a lecturer in physiology and director of the animal quarters at the University of Chicago.

"The pictures printed in the Chicago newspaper of purportedly tortured dogs were in fact either fakes or misrepresentations," Dr. Brewer said, "for the dogs, many of which had figured in some of the leading medical experiments leading to new cures for human and animal ills, as well as in tests of new 'miracle drugs', were not suffering. There was no 'torture' whatever inflicted by me or my associates." Dr. Brewer stated that the articles and pictures decidedly damaged him as a doctor of veterinary medicine, as a teacher, lecturer, and writer.

Dr. Brewer demanded a retraction from the offending newspaper, whose editors, he said, "responded by sending a special feature writer to his laboratories with the proposal that he 'even things up' by writing a series of articles for that publication or one of its affiliates on 'the good things' the doctor was doing"

Dr. Brewer's suit was the second million dollar libel action filed against the Chicago newspaper within ten days, as the result of that paper's campaigns against a bill before the Illinois General Assembly to provide that condemned animals from the pounds in the state he made available to medical

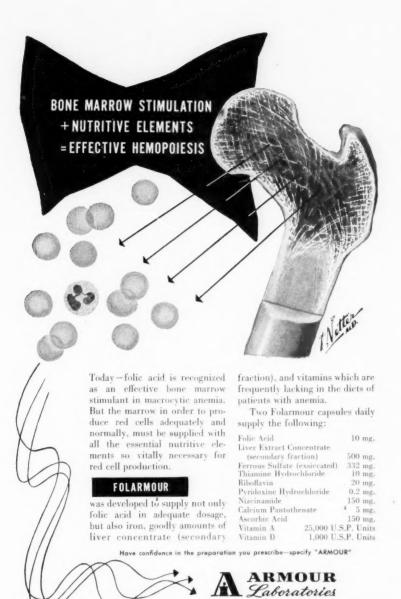
institutions. Dr. Virgil H. Moon of Wake Forest College's School of Medicine in North Carolina filed suit for a million dollars last week as the result of the newspaper printing an article which represented his views as being that animal experimentation is useless. In his complaint Dr. Moon stated that the newspaper had "maliciously misrepresented his views on animal experimentation" when on May 24 and May 29, 1949, it carried articles quoting him as saying that the medical profession indulges in "useless dog tortures."

These newspaper articles were further elaberations and distortions, Dr. Moon said, of an article printed on August 27, 1944, in the same paper based on an interview with a newspaperman who was "determined to get a story from me discrediting medical experimentation and reflecting upon the use of animals." Dr. Moon pointed out that the article said exactly the opposite of what he said in the interview. After the article first appeared, Dr. Moon wrote the editor demanding a correction but none was made.

A good example of the reticence of the medical scientist, Dr. Moon did not pursue the matter further until antivivisectionist leaders thoughout the country jumped to the humiliating conclusion that he was an ally and widely used the distorted article in their publications. During the last five years, Dr. Moon and his attorneys have been kept busy writing denials and demands for retractions as one reprint after another has appeared.

After Dr. Moon protested, however, the antivivisectionists continued to feature the article with an overprint indicating that it must be true since Dr. Moon had never sued for damages as the result of its original publication. By this time though the statute of limitations had run on the original publication, and it was not possible to file suit. "When the Chicago newspaper again carried substantially the same story recently," Dr. Moon stated, "I had no alternative but to file suit for damages. A vicious lie started five years ago refuses to be put down in any other fashion."

Any association with the antivivisectionists is particularly humiliating for Dr. Moon since the research for which he has been hailed



was done on dogs. Dr. Moon is credited with findings which have proved of benefit to thousands of war veterans who were victims of

battlefield shock.

According to John F. Sembower, counsel for the National Society for Medical Research, the members of the newly-formed Legal Committee for Medical Research will perform "minute man duty" throughout the country in protecting medical researchers against the character assassination to which they have been subjected by "fanatical anti-vivisectionists."

"The average citizen often is too busy to give critical judgment to the source of criticism, and consequently real damage is inflicted upon the reputations of many of the most heroic and tireless workers, in the laboratories for human, and even animal, welfare," Sembower

said.

"Since earliest times the Anglo-American system of justice has given a swift and sure remedy at common law for defamation of character, and now there are many criminal statutes on the books," he explained. "This will be invoked relentlessly and tirelessly in behalf of the medical researchers."

Care will be exercised that there is no collision whatever with equally well established legal doctrines of freedom of fair comment. "Practically every newspaperman knows the boundaries in this field and they do not handicap him in his work," it was explained. "The doctors are not even concerned with so-called 'borderline cases,' but must take steps to prevent unconscionably flagrant violations."

The membership of the legal committee includes the attorneys and counsel of leading colleges, universities, and medical institutions throughout the country, and representatives are located in every state, it was explained.

### NEW FINDINGS IN LIP CAN-CER TOLD BY ARMY DENTIST

"Sensitivity to cancer of the lip, regardless of sunlight factors, may be determined by the color of eyes and hair, as well as complexion," according to Lieutenant Colonel Joseph L. Bernier, Chief, Dental and Oral Pathology Section, Armed Forces Institute of Pathology, in a paper read before the Dental Faculty of the Royal College of Surgeons in London, England.

Colonel Bernier, who was recently elected to a Fellowship in Dental Surgery in the Royal College of Surgeons, has for over two and a half years been conducting a study on World War II soldiers with cancer of the lip, in conjunction with Mrs. M. L. Clark, Chief Statistician at the Institute. He had revealed earlier this year that of 528 lip cancers among white soldiers, the majority of patients were of fair or ruddy complexion. In his paper, "Carcinoma of the Lip—An Analysis of 835 Cases," Colonel Bernier said that supplemental research has disclosed that:

- 1. Blue or grev eyes, blonde or brown hair, and fair or ruddy complexion were found in the majority of more than 500 World War II soldiers with cancer of the lip. These combinations held regardless of the geographic regions in which the soldiers had lived, although 72 per-cent were born south of the 40-degree parallel, where the incidence of skin cancers is unusually high.
- 2. These findings, together with the extremely low percentage of lip cancer in Negro soldiers (who have abundant pigmentation and thickness of skin) indicates that an absence of protective pigment and thinness of skin may be influencing factors in persons subjected to prolonged sunlight.
- 3. Approximately 90 percent of both "indoor" and "outdoor" workers had fair or ruddy complexions. Since former indoor workers had periods of relatively long exposure to sunlight during Army service, it is possible that the "sunburn" wavelengths of solar radiation (3200 angstrom units or less) are a factor in developing lip cancer in persons who lack sufficient protective pigmentation or whose outer skin covering is thin.
- 4. Seventy-six percent of the soldiers served for six months or longer in United States areas which received 60 to 85 percent of the possible annual sunshine, and 62 percent served in tropical or subtropical areas for at least six months.
- 5. Of 375 patients who were followed after treatment, 343 were living and free from cancer at the end

of three years, making a three-year cure rate of 91.5 percent. The cure rate for five years was 82.1 percent.

6. Approximately 83 percent of the surgical and biopsy specimens showed changes in the skin and/or nucous membrane of the lip, which are usually associated with age changes in normal skin and nucous membrane.

Although the survey is not completed as yet, an important observation seems to be that lip cancer is usually of low-grade malignancy and most often occurs in tissue in which the degenerative changes of age are seen. Colonel Bernier also stated that although heredity may appear as an important factor in the occurrence of lip cancer, this is apparently centered about the absence or presence of protective pigmentation and the thinness of the skin.

## INTERNATIONAL ACADEMY OF PROCTOLOGY

Officers elected for the coming year are: President, Earl J. Halligan, Jersey City, N. J.; President-elect, Caesar Portes, Chicago, Ill., 1st Vice-President, H. A. Springer, Cincinnati, Ohio: 2nd Vice-President, Edgar M. Scott, Jr., Birmingham, Ala.; 3rd Vice-President, I. Norman Albert, Johnston City, Ill.; Secretary, Alfred J. Cantor, Flushing, N. Y.; Treasurer, William Lieberman, Brooklyn, N. Y.; Chairman of Board of Trustees (temporary), Earl J. Halligan, Jersey City, N. J.

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Dr. Alfred J. Cantor was unanimously acclaimed the first president of the Academy in recognition of having organized and car-



ried on the work of the Academy for the first year single-handedly.

Membership in the Academy is open to those who are specializing in Proctology or allied fields. Further information and application blanks may be obtained by writing to the Academy, 43-55 Kissena Blvd., Flushing, N. Y.

### FROHLICH GETS JOB

Johnson and Johnson, Brunswick, New Jersey, have appointed L. W. Frohlich and Company their advertising agency, to handle products of their Professional Service Division for promotion to the medical profession. Products include: Red Cross Cotton, Red Cross Adhesive Tape, BAND-AID Adhesive Bandages, Red Cross Sterile Gauze Pads, and Red Cross Cotton Balls.

#### DR BUCKMAN JOINS PARKE-DAVIS MEDICAL STAFF

Appointment of R. J. Buckman, M. D., to the medical staff of the sales and promotion division of Parke, Davis & Company, Detroit, Michigan, has been announced by H. J. Loynd, Vice-President of the Company in charge of Sales and Promotion.

Dr. Buckman received his Doctorate in Medicine from the University of Louisville School of Medicine in 1930, Prior to coming with Parke-Davis, he spent 10 years in the practice of general medicine in his home state of Kentucky, and in Tennessee; and 9 years in medical work in the pharmaceutical industry. With an ex-tensive background including experience in medical correspondence, medical literature, clinical investigation, and participations in the training of sales staffs, Dr. Buckman comes to Parke-Davis exceptionally well equipped for his assignment to the office of Medical Consultant.

### COGENAT

The National Drug Company of Philadelphia, manufacturers of pharmaceutical, biological and biochemical products for the medical profession, announces an addition to their line of hormone products with the introduction of Cogenat.

Advantages: Cogenat (for oral administration) is a potent and

well-tolerated estrogen. It will frequently relieve the physical symptoms of the estrogen-deficient patient and promptly restore the sense of well-being. Untoward sideeffects are seldom troublesome.

The conjugated estrogens in Cogenat are derived from natural sources, pregnant mare's urine. They are preserved in the water-soluble form in which they are excreted by the kidney. Unlike free natural estrogens, Cogenat is rapidly absorbed from the gastrointestinal tract and is not inactivated by the liver.

Action and Uses: Cogenat is effective in the treatment of estrogenic deficiencies ocurring at the menopause; in senile vaginitis; postpartum breast engorgement; functional uterine hemorrhage; female hypogenitalism; amenorrhea; in the male, palliation of local discomforts from prostatic carcinoma and its metastases may be obtained.

Dosage: 1.25 mg. to 3.75 mg. daily. Since responses to estrogenic therapy varies widely, fixed dosage schedules are impractical. Following the initial relief of symptoms a maintenance dosage just sufficient to provide continued relief is recommended.

How Supplied:
Cogenat Tablets (Green).... 0..625
mg., in bottles of 100 and 1000.
Cogenat Tablets (Orange) .... 1.25
mg., in bottles of 100 and 1000

#### SCHERING CLINICAL RE-SEARCH DIVISION APPOINT-MENTS

The appointment of W. Alan Wright, M. D. and Norman L. Heminway, M. D. to newly created positions of Associate Director of Clinical Research has been announced by Mr. Francis C. Brown, president of Schering Corporation, pharmaceutical manufacturers of Bloomfield, N. J.

Dr. Wright first received a degree in pharmacy from the Philadelphia College of Pharmacy and Science in 1939 and his Bachelor of Science degree in 1935 from Juniata College, where he majored in chemistry and biology. In 1939 he graduated with the degree of Doctor of Medicine from Temple University Medical School. After private practice and serving as a

principal medical officer with the Federal Trade Commission, he joined Schering's Division of Clinical Research in 1946. He is a member of the American Academy of Allergy and the Association for the Study of Internal Secretions. Dr. Wright now holds the position of Associate Director of Clinical Research with Schering.

Dr. Heminway received his Bachelor of Science degree in 1931 from Franklin and Marshall College and his degree of Doctor of Medicine from the University of Pennsylvania Medical School in 1935. After several years in private practice, Dr. Heminway entered the Army in 1941 where he served as chief Surgeon of the Greenland Base Command. Later, as Commander of the hospital ship USA-HS Wisteria, he attained the rank of Colonel. Upon completion of his Army service, he joined Schering in 1945 to establish and direct the Medical Service Department. Dr. Heminway now acts as Associate Director of Clinical Research as well as Administrative Assistant to Dr. Edward Henderson, Schering's Director of Clinical Research.

### BOOK NEEDS

CARE, the non-profit agency which has brought food to thousands of hungry people overseas, is now embarked upon a "food for the mind" program to rebuild the war-wrecked libraries of Europe and Asia, Paul Comly French, Executive Director, has announced.

Approved by the State Department's Advisory Committee on Voluntary Aid, the program aims to replenish the shelves of technical schools and libraries abroad with gifts of new American technical and scientific books, vitally needed for the education of college and professional students. Details are being carried out with the endorsement and cooperation of the U.S. Commission for UNES-CO, the Library of Congress, the American Library Association, and the U. S. Book Exchange. The plan works this way:

Libraries, universities and other educational institutions in 14 wardevastated countries are being asked by CARE to supply a list of their book needs. Through contributions from the American people, CARE will then fill those needs as closely as possible, by purchasing the best



# why you should change to

# RESMICON

mucoprotective acid-adsorbent

We suggest that you treat your peptic ulcer patients with Resmicon. You may well ask yourself (and us) why you should abandon the ordinary antacids in favor of Resmicon.

The answer is: The gain is great, from the point of view of heightened effectiveness in relief of pain, greater rapidity of healing, and total absence of side effects.

### The reasons for this statement? Here they are:

- 1 Resmicon is not an antacid in the usual sense of the term; it contains no alkalis or amphoteric gels. Resmicon has two ingredients: an insoluble, unabsorbable, non-toxic, ion-exchange polyamine resin; and purified natural gastric mucin.
- **2** By physical adsorption to the resin, the offending factors, hydrochloric acid and pepsin are rapidly removed from their sphere of noxious activity in the stomach and transferred to the alkaline milieu of the intestines where they can do no harm.
- 3 The mucin protectively coats the damaged gastric mucosa, prevents penetration of acid and pepsin, and facilitates healing.
- 4 Because of its unique mode of action, Resmicon does not cause any distressing side actions so commonly observed with other agents. Thus there are no acid rebound, alkalosis, renal calculi or chloride and phosphate deprivation, as occur with ordinary alkalis (e.g., sodium bicarbonate, calcium carbonate, magnesium oxide, etc.); and no colic or constipation, as may occur with antacid gels (e.g., aluminum hydroxide, silicates, amphoteric gels, etc.).

Resmicon is available in bottles of 84 tablets, each tablet containing 500 mg. anion-exchange polyamine resin and 170 mg. gastric mucin.

If you would like to know more about Resmicon, please write us for our comprehensive booklet.





Division Nutrition Research Laboratories Chicago 30, Illinois

books in those fields published in the United States. Contributions can be sent to CARE headquarters, 20 Broad St., New York, or to any CARE outlet throughout the country.

"This is the answer to the millions of books that were lost when Hitler started his book-burnings, when bombs destroyed whole libraries," Mr. French said. "CARE is responding to the challenge presented by the dearth of educational material throughout the world by adding books to the food and textile packages which may be sent abroad through CARE."

Selection of the books CARE purchases will be based upon lists compiled by a bibliography committee headed by Dr. Luther Evans, Librarian of Congress. Only new books are involved. No used books can be accepted. Through special arrangements with publishers, all of CARE'S costs of purchase and delivery overseas will be covered at the book publisher's list prices. The books will be in the English language. This follows definite educational trends abroad—85 percent of the requests for scientific and technical books received by UNESCO are for books printed in English.

Although CARE hopes to expand the program later, at present it is limited to special "priority" categories of books, and for delivery to institutions only, not individuals. The categories include: health and welfare; medical; dentistry; veterinary science; nursing; agricultural science; English language instruction; biology; chemistry; engineering; geology; library administration; mathematics; physics; physiology; psychology; sociology and statistics.

The countries to which CARE is offering the book deliveries are: Austria, Belgium, Czechoslovakia, Finland, Italy, France, Greece, Korea, Japan, the Netherlands, Norway, Poland, Great Britain, the three Western zones of Germany and all Berlin.

Individuals or groups can contribute funds in any amount for the CARE book program. All contributions are tax-exempt. Donors of \$10 or more may designate the country, the institution, and the category (but not the title) of the book to be sent. They will receive the usual CARE receipt, signed by the recipient. Donations under \$10

will be pooled in CARE's general book relief fund, and donors will receive a CARE acknowledgment, but not a signed receipt.

### UNITED CEREBRAL PALSY ASSOCIATION

The United Cerebral Palsy Associations, Inc., has appointed Mrs. J. Howard Brinckerhoff to head its current program of expansion and national affiliation of its member units throughout the United States. Mrs. Brinckerhoff will work directly with local groups which have sprung up all over the country, spearheaded by parents determined to better personnel and medical treatment for their affected children. UCPA's purpose is to foster an improved public understanding of the fact that cerebral palsy is in most cases a purely physiological affection. The vast majority of cerebral palsied persons can be educated to be self-reliant citizens

The new UCPA Field Director has been engaged for the past eight years in enlisting lay leadership and in educational and organizational work for United Service to China. She has served on committees of the Dutch Reformed and Presbyterian Churches and of the Greater New York Federation of Churches, and has been active in the Girl Scouts of America, Inc., the Young Women's Christian Association, and in the Junior League. She is an alumna of the University of Illinois, and a member of Alpha Chi Omega, national women's fraternity.

### SCHERING GIVES DOCTORS TAX GUIDES

The "Schering Physicians' Income Tax Guide for 1950" is a new and up-to-the-minute edition of the popular compilation of information on how to prepare the doctor's income tax declaration and return. It is now being distributed free on request to the Medical Service Department of Schering Corporation, Bloomfield, New Jersey, according to Dr. John N. McDonnell, Schering's vice-president. Designed to meet the need of busy practitioners. every possible sination in the proper completion of income tax returns is covered clearly and concisely. It provides authoritative answers for everything from general tax return procedure to such problems as bad debts or the deductibility of reading matter for the physician's waiting room.

Prepared especially for physicians by tax experts Hugh J. Campbell and James B. Lieberman, and containing a special message to the physician from Mr. Francis C. Brown, Schering's president, the "Schering Physicians' Income Tax Guide for 1950" includes examples of filled-in tax returns, accompanied by lists of permissible deductions. The "Guides" are also being presented to physicians by Schering Professional Service Representatives, as a further service to the medical profession.

## FEDERAL SECURITY AGENCY

Public Health Service Division of Medical and Hospital Resources

A conference sponsored by six southeastern States was held in Atlanta, November 15-17, 1949 to discuss the problems which confront new hospitals.

Dr. John R. McGibony, Chief, Division of Medical and Hospital Resources said in his closing remarks that this Atlanta conference might be a prelude to similar sessions in other parts of the country, as the nation envisions the opening of hundreds of new hospitals at an accelerated pace during the next few years.

Sponsoring states were Georgia, South Carolina, Tennessee, Alabama, Florida and Mississippi. The meeting was presented in cooperation with the Division of Medical and Hospital Resources, U. S. Public Health Service. The primary purpose of the sessions was to acquaint State agency personnel with the myriad tasks confronting any hospital approaching the day when the first patients will be admitted.

The meetings were open to administrators and trustees of new hospitals in the region. Forty persons representing new hospitals were among 85 attending.

Among outstanding papers presented were "Personnel Problems, Policies and Sources" by H. Carl Rowland, Assistant Administrator, Spartanburg General Hospital, Spartanburg, South Carolina; "Legal Aspects of Hospital Operation" by R. F. Whitaker, Superintendent, Emory University Hospital, Emory University, Georgia, and "The Hospitals of the Property University, Georgia, and The Hospitals of the Property University, Georgia, and The Hospitals of the Property Control of the Property of the Prop



# Effective and Convenient ANTACID MAINTENANCE

Creamalin, the first aluminum hydroxide gel, readily and safely produces sustained reduction in gastric acidity. With Creamalin there is no compensatory reaction by the gastric mucosa, no acid "rebound," and no risk of alkalosis. Through the formation of a protective coating and a mild astringent effect, nonabsorbable Creamalin soothes the irritated gastric mucosa. Thus it rapidly

Creamalin liquid N.N.R. (peppermint flavored) in bottles of 8, 12 and 16 fl. oz.

Creamalin tablets (not N.N.R.), tins of 12, bottles of 50 and 200. Creamalin capsules (not N.N.R.), bottles of 24 and 100. Each tablet or capsule is equivalent to 1 teaspoonful of Creamalin liquid.

relieves gastric pain, speeds healing of peptic ulcer and helps to prevent recurrence. **Average dose:** Peptic ulcer, 2 to 4 teaspoonfuls (or tablets or capsules) with a little milk or water every two to four hours. Dyspepsia: 2 teaspoonfuls (or tablets or capsules) one-half to one hour after meals.

WINTHROP-STEARNS INC. New York 13, N. Y., Windsor, Ont.



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pital Administrator" by Marshall I. Pickens, The Duke Endowment, Charlotte, North Carolina.

### CIVILIAN INTERN PRO-GRAM ANNOUNCED BY AIR FORCE MEDICAL SERVICE

The U. S. Air Force Medical Service is offering commissions to 200 selected civilian interns in the United States to serve in the Air Force Reserve as first lieutenants on active duty with full pay and allowances, according to an announcement by Major General Harry G. Armstrong, the USAF Surgeon General.

Eligible to receive commissions are physicians who will be graduated from approved medical schools between January 1 and July 1, 1950, and who are to begin internships between those dates in approved civilian hospitals.

Physicians who are so commissioned will serve two years of active duty for each year of internship acomissioned U. S. Air Force Reserve officers at Air Force medical installations.

Information concerning the intern program may be obtained by written request to deans of medical schools or the Officer's Procurestrong was sworn in as Surgeon General of the U. S. Air Force Force, Washington 25, D. C.

### GENERAL ARMSTRONG SWORN IN AS AIR FORCE SURGEON GENERAL

Major General Harry G. Armstrong was sworn in as Surgeon General of the U. S. Air Force Medical Service. The Air Judge Advocate General, Major General Reginald C. Harmon, administered the oath in the office of USAF Chief of Staff, General Hoyt S. Vandenberg.

General Armstrong succeeds Major General C. Grow, who retired on November 30

General Armstrong, an authority on aviation medicine, was a winner of the Collier Award for aviation achievement in 1939. He first took an interest in the relation of medicine to flying while in private practice in Minneapolis, Minnesota, after his graduation from the University of Louisville Medical School in 1925.

Both General Armstrong and General Grow were assigned to the Engineering Division of the Air Corps at Wright Field, Dayton, Ohio, in 1934, when they became active in establishing an aviation medicine research laboratory that grew into the present-day Aero Medical Laboratory there.

General Armstrong was director of the Aero Medical Laboratory for six years, and was responsible for its rapid growth and many ac-

complishments.

General Armstrong initiated research into the effects of flying on the body while director of the laboratory. He made the first detailed study of the effect of noise, and changes in altitude on the ear, and pioneered in demonstrating the effects of lack of oxygen at progressively higher altitudes.

He adapted a mask for aircrews designed by Doctors Ed Boothby and W. Randolph Lovelace, II, of the Mayo Clinic; and initiated development of the oxygen system

now in use in aircraft.

General Armstrong's recommendations for improved aircraft design and making flight at high altitudes safer and reducing pilot fatigue, for the use of protective clothing and equipment, were the basis for his being awarded the Collier Award in 1939.

He prepared the medical specifications and did the test work on the first successful pressure cabin airplane, and personally participated in experiments to determine what happens when the cabin is suddenly decompressed at high altitude.

It was also in 1939 that General Armstrong published "Principles and Practices of Aviation Medicine," the first inclusive text on that subject. The book is not only a standard work for flight surgeons, but has been highly beneficial to airplane designers, pilots, and medical students.

While a Reserve officer in the Army Corps in 1929, he entered the Air Force School of Aviation Medicine, then at Brooks Field, Texas, as a student. It was there that he made the first free-fall parachute jump in medical records expressly to discover the sensations of a free fall. On this occasion he jumped at a height of 10,000 feet, but did not pull his rip cord to open the chute until he was at 3,000 feet.

During the war, General Armstrong served as Surgeon of the Eighth Air Force, based in England. Here he instituted the use of rest homes for combat crews, improved the protective clothing in use, and put into operation the first Central Medical Establishment. Here much of the research on frostbite at high altitudes, survival and air-rescue problems, and death from loss of oxygen supply was carried out.

After the war, General Armstrong, while with the Office of Military Government in Berlin, visited every European country and studied advances made in medicine during the war years. He was one of the group which established an aeromedical laboratory in Heidel-

berg.

In 1946 he became Commandant of the School of Aviation Medicine at Randolph Air Force Base, Texas, where, in 1941, he had established the Research Section. As Commandant, General Armstrong began research in the newest medical field when he organized the Department of Space Medicine. This was done in anticipation of possible en incering developments which might make it practical to design manned rocket ships capable of flight beyond the earth's atmosphere.

In July, 1949, General Armstrong became Deputy Surgeon

He has received numerous degrees, including the Master of Arts in Internal Medicine from the University of Cincinnati; Master of Science in Physiology from the University of Toronto, Toronto, Canada; and has twice been given an honorary Doctorate of Science, once by the University of South Dakota and once by the University of Louisville. He has been awarded the Legion of Merit, with oak leaf cluster, the Cruses de Guerre, with palms, of Belgium and France, and the Order of the British Empire.

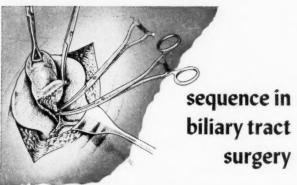
General Armstrong is a native of De Smet, South Dakota. He is married to the former Mary E. Sutherland, of Harrodsburg, Kentucky, and has two children, a daughter, Jeff, aged 21, and a son, Bradley,

aged 19.

### ROSENSTOCK MEMORIAL FOUNDATION ANNOUNCES FELLOWSHIP PLAN FOR 1951

1950 Fellowship Award Winners Named

The Rosenstock Memorial Foundation, Inc., a philanthropic Foun-





### preoperatively-Decholin

brand of dehydrocholic acid stimulates an abundant flow of thin bile, helping to "clear the arena" for surgery by the removal of inspissated bile, mucus, small stones and other accumulations from the choledochus. This powerful hydrocholeretic action also produces functional distension of the gallbladder and ducts, aiding in identification and surgical procedure.



### postoperatively-Decholin

provides an effective means of flushing out the biliary tract. Used together with antispasmodies such as atropine and nitroglycerin, Decholin helps to remove blood clots, residual debris and hidden, small calculi. This method, recently re-emphasized by Best, 1 is useful with or without T ubed drainage. In reflex biliary stasis, Decholin serves to prompt an adequate secretion of bile.

For more rapid and intense hydrocholeresis, *Decholin Sodium*, brand of sodium dehydrocholate, is given intravenously, followed by a course of *Decholin* tablets.



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brand of dehydrocholic acid

Decholin (brand of dehydrocholic acid) Tablets of 3 % grains, in bottles of 25, 100, 500 and 1000,

Decholin Sodium (brand of sodium dehydrocholate) 20% solution, in ampuls of 3 cc., 5 cc. and 10 cc., boxes of 3 and 20.

1. Bers, B. R.: Ann. Surg. (28, 148 (Sept.) 1948.

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AMES COMPANY, INC. BLEHART, INDIANA

dation for the purpose of fostering individual medical research without regard to race, color, creed or sex, in accordance with its announcement of September 15th, 1949, is pleased to announce the award of a Fellowship in Research to: Dr. Marvin F. Levitt, of Mt. Sinai Hospital.

A special award, for educational purposes, was made by the Rosenstock Foundation Board to: Dr. Johnson C. S. Chu, of N. Y. U., Bellevue Medical Center.

The Rosenstock Foundation will offer for 1951 two fellowships in the amount of \$3,000 for one year for the support of individual medical research to be conducted in a hospital in greater New York with Medical School affiliations. Fellowships may be granted either for full time or part time medical research.

Fellowships will be limited to those who apply within three years of the completion of internship or residency, and applications must be endorsed by the Director of the hos pital where it is proposed that the research will be conducted.

Applications may be made in any form that the applicant may desire outlining the nature of the work to be undertaken and the qualifications of the applicant. After endorsement by the Director of the hospital, the application should be forwarded to the Foundation, at 42-16 West Street, Long Island City 1, New York.

To save time for the Medical Committee in order to expediate the announcement of awards, it would be appreciated if applications were furnished in triplicate.

Applications should be received by November 1, 1950, for review by the Medical Committee, consisting of Dr. William Thalhimer, Chairman, Dr. Martin G. Vorhaus, and Dr. Edgar G. Miller.

P.S. We urgently request a tear sheet of this article when it appearc and will appreciate your attention to this matter.

# FEDERAL SECURITY AGENCY

Public Health Service Washington, D. C.

Appointment of Louis F. Warrick to the Public Health Service, Federal Security Agency, as Senior Sanitary Engineer in charge of an extensive water pollution control research program, was announced today by Federal Security Administrator Oscar R. Ewing.

Mr. Warrick will be associated with the nationwide program being conducted by the Public Health Service to alleviate water pollution conditions which are threatening the quality and use of this country's water resources.

As Chief of the Technical Services Branch of the Water Pollution Control Division, Mr. Warrick will work closely with those other Federal agencies principally concerned with water pollution control, and with interested State, educational, private and industry groups. He will be responsible for integrating all technical and research aspects of the Public Health Service water pollution control program.

Mr. Warrick is a graduate of the University of West Virginia, where he received his Bachelor of Science degree in Chemical Engineering, and of Cornell University, where he received a Master of Science degree in Sanitary Chemistry and Engineering.

For the past 24 years Mr. Warrick has been associated with the Wisconsin State Department of Health. His last position with that agency was as Director of the Bureau of Sanitary Engineering.

He is registered in Wisconsin as a professional engineer, and is a member of many professional societies, including: Conference of State Sanitary Engineers, Upper Mississippi Board of Engineers, the Federation of Sewage Works Association, American Chemical Society of Wisconsin, American Water Works Association, and the American Public Health Association.

Mr. Warrick has served as a member of the Wisconsin State Committee on Water Pollution since 1927 and, until coming to Washington, was Executive Secretary of that body.

For many years, Mr. Warrick has had a national reputation in the field of industrial waste and sewage treatment. He has served as chairman of a number of committees concerned with water pollution problems. He is the author of numerous articles relating to industrial wastes and sewage treatment problems which have appeared in technical and trade journals over the past 20 years.

Mr. Warrick is 47, married, and the father of two daughters and a son. He was born in Anderson, Indiana, and now lives at 105 West Woodbine, Chevy Chase, Maryland.

### SAHYUN OPENS NEW LAB IN CALIFORNIA

Dr. Melville Sahyun, formerly vice-president and director of research of the Frederick Steams and Co., Division of Sterling Drug Inc., has announced the opening of Sahyun Laboratories at 316 Castillo Street here. The laboratories are engaged in research in medicinal chemistry, nutrition, biochemistry and pharmaceutical products in general. Dr. Sahyun's chief assistant is Jack Faust, who received his Ph.D. in organic chemistry from the University of Michigan.

from the University of Michigan.

For Stearns, Dr. Sahyun's first major investigation was the development of the first commercial process for the manufacture of crystalline insulin. Subsequently he developed two prolonged acting insulins, clear protamine zinc insulin and camphor insulin. In 1935 he began an investigation on amino acids that culminated in the development of the first amino acid preparation for parenteral administration in man, also Essenamine. He also developed the process for the manufacture of ferrous gluconate and potassium gluconate.

A graduate of the American University of Beirut in 1916, Dr. Sahyun came to this country in 1923. His first work in the United States was in biochemical investigations on insulin and cancer at the Santa Barbara Cottage Hospital, Santa Barbara. During that time he published 12 scientific papers on insulin and carbohydrate metabolism, and developed one of the earliest and most accurate methods for the standardization of this horpotene.

Dr. Sahyun received his M. S. degree from Stanford University in 1929 and was awarded the Ph. D. degree in biochemistry and physiology by the same university in 1931. In that year he was appointed a research associate of the Food Research Institute of Stanford University.

Dr. Sahyun is a member of the American Chemical Society, the Chemists, the Society of Experimental Biology and Medicine, the American Association of Pharmacy, Sigma Xi, New York Academy of Sciences, and a Fellow of the

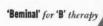


The 'Beminal' family provides a choice of five distinctive forms and potencies for the effective treatment of vitamin 'B' deficiencies. Each is designed to fill a particular need.

- 'Beminal' fortified with Iron, Liver and Folic Acid Capsule No. 821 is suggested for the treatment of iron deficiency anemias, certain macrocytic anemias and as adjunctive therapy in pernicious anemia.
- 'Beminal' with Iron and Liver Capsule No. 816 is recommended for the treatment of the various types of iron deficiency, occurring either as frank hypochromic microcytic anemia or as the less pronounced anemia of nutritional origin.
- 3. 'Beminal' Forte with Vitamin C Capsule No. 817 is suggested when there is severe depletion of the patient's nutritional stores due to either prolonged dietary inadequacy or nutritive failure as a result of organic disease.
- 4. 'Beminal' Forte Injectable (Dried) No. 495 provides, when reconstituted, a high concentration of important vitamin B factors for intensive therapy.
- Beminal' Tablets No. 815 may be of value if the vitamin B complex deficiency is mild or subclinical.

Ayerst, McKenna & Harrison Limited 22 East 40th Street, New York 16, N. Y.









American Association for the Advancement of Science. He is editor and author of two books, "Outline of the Amino Acids and Proteins" and "Proteins and Amino Acids in Nutrition," as well as more than 60 scientific papers.

### S-W RESEARCH INSTITUTE PROMOTES DR. DENNIS

Dr. E. Westervelt Dennis, formerly associate director, has been appointed director of the biological division of the Sterling-Winthrop Research Institute, a division of Sterling Drug Inc. He succeeds Dr. Lloyd Miller, who is leaving the Institute to become director of

Revision of the United States Pharmacopea.

The promotion was announced here by Dr. Maurice L. Tainter, vice-president and director of the Institute, now in process of moving into its new laboratory building America's most modern pharmaceutical institute.

As head of the biological division, Dr. Dennis directs the work of the research sections of biochemistry and endocrinology, pharmacodynamics, and chemotherapy. He retains the position as head of the chemotherapy section.

The combined staffs of these three sections test the action of new compounds against disease, study antiseptics, make pharmacological tests with new drugs studying physiological properties of analgesics, antibiotics and antihistamines among others, investigate drug metabolism, and conduct research in nutrition, vitamins, proteins and hormones.

Dr. Dennis figured prominently in recent research on drugs for combatting amebiasis and field tests with Aralen, the new and powerful antimalarial. His findings, with associates, have been published by the American Journal of Tropical Medicine.

During World War II, he performed extraordinary service in making vaccines and anti-typhus serums for the civilian population of Lebanon. For this work, he and Dr. D. A. Berberian were awarded the Medaille d' Honneur Merite by the President of the Lebanese Republic in 1943. Dr. Berberian is at present group leader in the Institute's chemotherapy section. At the time, Dr. Dennis was head of the Department of Bacteriology and Parisitology of the American University of Beirut, Lebanon, and Dr. Berberian was an associate professor.

Dr. Dennis was associated with the American University from 1931 to 1935, when he first joined the nated from the University of Oklastaff of the Institute. He was gradhoma City, his birthplace, and re ceived his Ph.D. from the University of California in 1931. He served as instructor in biology at the U. of C. in Los Angeles in 1930.

Dr. and Mrs. Dennis reside at 48 Willett Street, Albany. They have two sons, LeBaron, 17, at Dartmouth, and Robert, 15, at the Milne School of the Albany State Teacher's College.

Dr. Miller, whom Dr. Dennis succeeds, was honored at a fare-well dinner in Albany, December 14, attended by top executives of the Institute and by Dr. Theodore G. Klumpp, president of Winthrop-Stearns, Inc. He was presented with matched traveling bags to go with a brief case previously given him by his divisional staff.

Eight (8) new grants for research on problems of human nutrition were announced recently by Dr. E. Gifford Upjohn, the Foundation's President. The new grants, amounting to \$55,505.00 become effective on January 1, 1950 and bring to \$240,801.00 the total amount appropriated by this non-profit Foundation for grants-in-aid of research on the significance of the vitamins and other mutritional factors to human health and resistance to disease. Since 1946, an additional \$77,333.00 has been appropriated by the Foundation for a number of educational projects for the profession and the laity.

The eight (8) new research grants to become effective on January 1, 1950 include:

Dr. Bacon F. Chow, The Johns Hopkins University, School of Hygiene and Public Health; \$5,000 to study the value of vitamin B<sub>12</sub> in promoting growth of infants on diets restricted because of medical reasons, of apparently healthy in-

fants on normal diets and on chronically ill older children.

Dr. William J. Darby and Dr. Edgar Jones, Vanderbilt University, School of Medicine: \$21,000 for a three-year study of the effects of vitamin B<sub>12</sub> and of the pteroylglutamates (folic acid) on the blood forming organs and the circulating blood in the human, and the determination of the requirements of man for these vitamins for the maintenance of normal blood cell and hemoglobin values, as well as for the prevention of nervous disorders (combined system disease) in patients with pernicious anemia.

Dr. Benjamin M. Kagan, Michael Reese Hospital, Chicago, Illinois; \$7,500 for studies of vitamin A metabolism in man in health and disease and particularly of disturbances in vitamin A metabolism observed in certain diseases of the kidney and of the liver.

Dr. R. W. Luecke, Michigan State College, Dept. of Agricultural Chemistry; \$3,000 for the study of the effects of low intakes of certain of the B vitamins during pregnancy on the health and livability of the new born, using the pig as the experimental animal.

Dr. Elaine P. Ralli, New York University, College of Medicine; \$3,605 for continuation of studies on the relation of certain of the B vitamins, particularly pantothenic acid, to the functions of the adrenal glands and of the pituitary gland.

Dr. Tom D. Spies, Northwestern University, Department of Nutrition and Metabolism; \$5,400 for studies on the effects of vitamin B<sub>12</sub> on the bone marrow and the circulating blood of patients with nutritional macrocytic anemia and sprue.

Dr. Richard W. Vilter, University of Cincinnati, College of Medicine; \$5,000 for the study of pyridoxine (vitamin B<sub>6</sub>) deficiency in man and its effective treatment.

Dr. Heinrich Waelsch, New York State Psychiatric Institute; \$5,000 for continuation of studies on glutamic acid and glutamine metabolism

### NATIONAL GASTROENTER-OLOGICAL ASSOCIATION 1950 AWARD CONTEST

The National Gastroenterological Association again takes pleasure in DRAINAGE PLUS





**CHOBILE**°

CHOBILE supplies the active principles of natural bile to improve the functions of the alimentary tract, plus Ketocholanic Acids to flush the biliary passages with a copious flow of low-viscosity bile.

In chronic indigestion and constipation of biliary origin, in ascending cholangitis and cholecystitis, many physicians prescribe CHOBILE for nonsurgical drainage of the biliary tree and improvement of digestion.

Each CHOBILE Tabule contains  $1\frac{1}{2}$  grs. Cholic Acid (conjugated as sodium taurocholate and sodium glycocholate), plus  $1\frac{1}{2}$  grs. Ketocholanic Acids. Samples on request.

IRWIN, NEISLER & CO.



DECATUR, ILLINOIS

announcing its Annual Cash Prize Award Contest for 1950. One hundred dollars and a Certificate of Merit will be given for the best unpublished contribution on Gastroenterology or allied subjects. Certificates will also be awarded those physicians whose contributions are deemed worthy.

Contestants residing in the United States must be members of the American Medical Association. Those residing in foreign countries must be members of a similar organization in their own country. The winning contribution will be selected by a board of impartial judges and the award is to be made at the Annual Convention Banquet

accent on

of the National Gastroenterological Association in October of 1950.

Certificates awarded to other physicians will be mailed to them. The decision of the judges will be final. The Association reserves the exclusive right of publishing the winning contribution, and those receiving Certificates of Merit, in its Official Publication, THE REVIEW OF GASTROENTEROLOGY.

All entries for the 1950 prize should be limited to 5,000 words, be typewritten in English, prepared in manuscript form, submitted in five copies accompanied by an entry letter, and must be received not later than 1 June 1950. Entries

should be addressed to the National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.

## SCHERING PROMOTES RENDELL

According to an announcement made by Dr. John N. McDonnell, vice president, Schering Corporation, pharmaceutical manufacturers of Bloomfield, New Jersey, Mr. Harry Rendell of West Somerville, Mass., has been designated Eastern Division Manager of the Domestic Sales Division. For the past three years Mr. Rendell has been Eastern Division Supervisor, with head-quarters in Boston.

Mr. Rendell graduated from the New England School of Pharmacy and is a registered pharmacist. Prior to joining Schering in 1944, he had been associated with other organizations as a field representative. He served as a Schering professional service representative in the Boston area and in 1945 was appointed Eastern Division Supervisor. Mr. Rendell's promotion is another step in the program of expansion of Schering service to the medical and pharmaceutical profes-

therapeutics!
vi-syneral therapeutic

new! new! new!

Vi-Syneral Therapeutic supplies in intensive therapeutic dosage not only the vitamina usually included in the therapeutic type of preparation, but also liver fractions, choline, inositol, folic acid... and eight nutritive minerals... based upon the original nutritional concepts of Dr. Casimir Funk... that vitamins should be given with minerals because they are functionally interrelated. The physician and surgeon, therefore, can anticipate results superior to those obtained with less complete formulas.

each dark celered capsule contains:		each light colored capsule centains:	
Vitamin A (natural)	25,000 Units	Choline	20 mg.
Vitamin D (natural)	1,000 Units	Inositol	10 mg.
Ascorbic Acid (C)	150 mg.	d-Calcium Pantothenate	15 mg.
Folic Acid	1.76 mg.	Calcium (as 1.54 Ga di-cale phosphate)	160 mg
Thiamine HCl (B1)	15 mg.	Phosphorus	132 mg
Niacinamide	150 mg.	Iron	15 mg.
Riboflavin (B2)	10 mg.	Copper	1.5 mg.
Pyridoxine HCl (B <sub>6</sub> )	5 mg.	Manganese	1.0 mg.
Alpha-Tocopherol (E)	10 mg.	Magnesium	1.0 mg.
Liver Fractions*	200 mg.	Zinc	1.0 mg.
*B complex factors derived from 1.1 Gm. of layer		Iodine	0.1 mg.

Suggested dose: One dark and one light colored capsule daily.

Prescription packages of 30, 50 and 100 capsules

Samples, literature from

u. s. vitamin corporation

casimir funk laboratories, inc. (affiliate)

### STUCKER APPOINTED SCHERING ADVERTISING MANAGER

Mr. Perry L. Stucker has been appointed Advertising Manager of Schering Corporation, pharmaceutical manufacturers of Bloomfield, New Jersey, according to Dr. John N. McDonnell, vice president. Mr. Stucker has been Division Manager of the company's Southern Division.

Mr. Stucker has been associated with Schering since 1939. After a number of years' experience in retail pharmaceutical practice and as field Representative in the Middle West, in 1941 he entered the Domestic Sales Department of Schering in Bloomfield. For three years, in World War II, he served in the U. S. Army, and after his return he was appointed Southern Division Supervisor.

Mr. Stucker graduated from Valparaiso University, Indiana, where he majored in Pharmacy. He is a registered pharmacist. His promotion is another step in the Schering program of expansion.



HABIT TIME BOWEL MOVEMENT

Throw

ONE PINT

PKG. 1896

# Petrogalar Aqueous Suspension of Mineral Oil

MUSEUM TO THE THEORY OF THE THEORY

Plain

DIRECTIONS: Adults, one table

SHAKE WELL



NEW MICRONIZED PENICIL-LIN INHALER INTRODUCED BY WINTHROP-STEARNS

A piston valve inhaler for inhalation therapy with Micronized Crystalline Penicillin G is now available through Winthrop-Stearns Inc.

The piston-valve inhaler consists of four pieces, a cartridge with a soft plastic cap containing pulverized penicillin, a discharge chamber base into which the cartridge is placed after its cap is removed, a nosepiece for nasal inhalation and a mouthpiece for oral inhalation.

Each inhaler assembly is supplied with three cartridges of 100,000 units of Micronized Crystalline Penicillin G. Sodium. Refill cartridges come three to the vial and four vials to the box. The entire inhaler assembly cartridge is packaged in a plastic envelope.

The administration of Micronized penicillin by the piston inhaler assures an accurate dose with each application and is optimally distributed over the affected area, according to company literature. In crystalline form, it does away with the need for refrigeration as is the

case with penicillin solutions, is less costly and wasteful than the aerosolization with oxygen and eliminates the time consumed by manual vaporization.

Micronized penicillin may be applied therapeutically in cases of infectious rhinitis, nasopharyngitis, laryngitis and bronchitis caused by organisms susceptible to the action of penicillin. It has been found to reduce infectious pulmonary complications following thoracic surgery.

# MUCILOSE COMBINED WITH CASCARA NOW AVAILABLE

Winthrop-Stearns Inc. Combines Two Popular Laxatives to Produce New, Mild Remedy

Mucilose has been combined with Cascara Granules by Winthrop-Stearns Inc. to form a new and "extremely mild laxative," according to an announcement made here by the pharmaceutical manufacturer.

The normal peristaltic action induced by the Mucilose bulk has been reinforced by the action of cascara in this new laxative, the company stated. Physicians have found that some patients do not obtain sufficient stimulus from bulk laxatives alone, and it is for this refractory group that mucilose with cascara provides a mild yet effective treatment for constipation.

The addition of cascara to this basically bulk laxative also speeds up the action of the Mucilose, according to the firm's literature. With the addition of cascara by Winthrop-Stearns to Mucilose a therapeutic dose starts the evacuation in eight hours and it remains gently effective until the bulk of mucilose passes through the large intestine, which requires a total of about 36 hours.

Mucilose with Cascara Granules is packaged in 4-ounce metal cans. Mucilose granules and flakes continues to be available in 4-oz.

and 10-oz. cans.

### NEW PENICILLIN PRODUCT

Winthrop-Stearns, Inc., is now offering Procaine Penicillin G in Oil with 2% Aluminum Monostearate, Fortified with Potassium Penicillin G. Crystalline. Each unit contains 400,000 units of penicillin per cc and is packaged in vials of 10cc, sufficient for ten doses.



OF COURSE

# **ELIXIR MESOPIN**

### IS COUNCIL ACCEPTED!!



antispasmodic-highly selective in its action-in a liquid form.

Elixir Mesopin permits the administration of a proven gastrointestinal

It may be prescribed alone or in combination with many other commonly used drugs.

In digestive tract pain due to spasticity and hyperactivity, Mesopin provides prompt relief with virtual freedom from the undesirable side effects of atropine and belladonna. Effective relief of gastrointestinal spasticity may be obtained in such conditions as peptic ulcer, dyspepsia, flatulence, biliary disease, and constipation.

Supplied on prescription in 16-ounce bottles, each tecspoonful contains 2.5 mg. Mesopin, the equivalent of one Mesopin tablet.

Dosage: Adults, one to two teaspoonfuls; Infants, 15 to 20 drops.

Mesopin Tablets (2.5 mg.) also available.

# ELIXIR MESOPIN ENDO

THERAPEUTIC VEHICLE . SELECTIVE GASTROINTESTINAL ANTISPASMODIC

ENDO PRODUCTS INC. . RICHMOND HILL 18, N. Y.

### compatible with the

# deficiency theory

### in the management of gastrointestinal

disorders. . .

Viodenum



"The treatment of . . . gastric ulcer and duodenal ulcer . . . is based on the supposition that the normal functions of the stomach and the duodenum are maintained by various biologically active substances, the absence of which favours ulcer formation."

\*Hubacher, O., Lancet, 251, 272 (1946).

"... not only were these patients relieved of their symptoms, but in all cases (8) included in this particular report there was roentgenologic evidence of ulcers having healed ... it is not expected that ... duodenal ... will prove to be a specific for peptic ulcer, for I do not believe that any single substance will ever be able to correct all the interacting factors responsible ... I am fully convinced, however ... the protecting mechanism inherent in duodenal ... would be invaluable in the treatment of ulcer."\*

\*Rivers, A. D., Am. J. Dig. Dis., 2, 189 (1935).

"A consideration of the natural course of ulcerative colitis led to the theory that in some cases the condition might arise as the result of a deficiency. Preliminary investigations suggested that the missing hypothetical factor might be present in or produced by the intestine. Feeding experiments . . . showed that remissions could be induced regularly by giving uncooked pig's small intestine by mouth . . . the results obtained with this treatment do not appear to be coincidental or psychological; they are compatible with the deficiency theory advanced . . ."

°Gill, A. M., Lancet, 2, (1945).

"Duodenal substance (Viodenum) was administered to thirty-five patients who had chronic ulcerative colitis... no other specific medication was used... the results obtained in 85 per cent of the patients were very favorable... the majority of the patients gained weight... felt better and ate better... duodenal substance (Viodenum) may be considered a very valuable aid in the therapy of chronic ulcerative colitis."\*

\*Streicher, M. H., J. Lab. Clin. Med., 33, 1633 (1948).

RAW duodenum desiccated and defatted at body temperature.

Provided in powder or ten grain tablets:

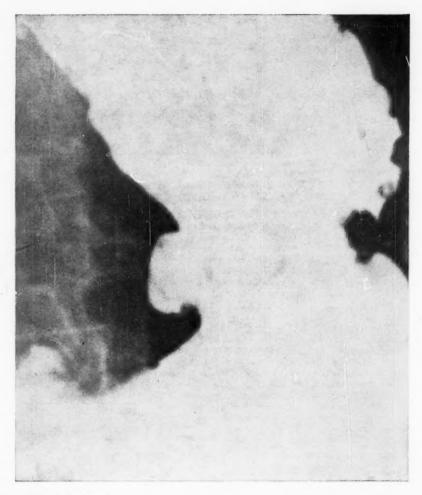
Literature available upon request

Viodenum

VIOBIN LABORATORIES



ulcerative coliti



A large benign chronic ulcer with steep side walls as seen in barium-filled shadow on the lesser curvature of the stomach.



When your patient is on a special diet, as in the management of peptic ulcer, gallbladder disease, obesity, etc., there may be insufficient fecal bulk for encouraging the normal peristaltic reflex.

**METAMUCIL**® is the highly refined mucilloid of a seed of the psyllium group, Plantago ovata (50%), combined with dextrose (50%).

SEARLE RESEARCH IN THE SERVICE OF MEDICINE